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Signed R. Mahoney

Dated 22 SEP 1999

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Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

1. Your reference — KR/JW/P32267

2. Patent application number
(The Patent Office will fill in his part) — **9905518.8**

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

SmithKline Beecham plc
New Horizons Court, Brentford, Middx TW8 9EP,
Great Britain

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation — S2000974002

4. Title of the invention — Novel Method and Compound

5. Name of your agent *(if you have one)*

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SMITHKLINE BEECHAM PLC
TWO NEW HORIZONS COURT
BRENTFORD
MIDDLESEX TW8 9EP

Patents ADP number *(if you know it)* — S2000974004

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer yes if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is named as an applicant, or
c) any named applicant is a corporate body
See note (d)

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Continuation sheets of this form	
Description	71
Claim(s)	
Abstract	
Drawings	

10. If you are also filing any of the following, state how many against each item.

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Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 1/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. We request the grant of a patent on the basis of this application

Signature K Rutter Date 10-Mar-99

12. Name and daytime telephone number of person to contact in the United Kingdom: K Rutter 01279 644396

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Novel Method and Compounds

This invention relates to a novel method for the treatment of conditions associated with a need for inhibition of glycogen synthase kinase-3 (GSK-3), especially diabetes, dementias, such as Alzheimer's disease, manic depression and cancer and certain novel inhibitors of GSK-3 used in such method.

GSK-3 is a serine/threonine protein kinase having a 47kDa monomeric structure. It is one of several protein kinases which phosphorylates glycogen synthase (GS) (Embi et al Eur. J. Biochem. **(107)** 519-527 (1980)). Two isoforms are found in mammalian cells: α and β. Both isoforms phosphorylate muscle glycogen synthase (Cross et al Biochemical Journal **(303)** 21-26 (1994)) and these two isoforms show good homology between species (e.g. human and rabbit GSK-3α are 96% identical).

Type II diabetes (or Non-Insulin Dependent Diabetes Mellitus, NIDDM) is a multifactorial disease. Hyperglycaemia is due to insulin resistance in the liver, muscle and other tissues coupled with inadequate or defective secretion of insulin from pancreatic islets. Skeletal muscle is the major site for insulin-stimulated glucose uptake and in this tissue, glucose removed from the circulation is either metabolised through glycolysis and the TCA cycle, or stored as glycogen. Muscle glycogen deposition plays the more important role in glucose homeostasis and Type II diabetic subjects have defective muscle glycogen storage.
The stimulation of glycogen synthesis by insulin in skeletal muscle results from the dephosphorylation and activation of glycogen synthase (Villar-Palasi C. and Larner J. Biochim. Biophys. Acta **(39)** 171-173 (1960), Parker P J et al Eur. J. Biochem. **(130)** 227-234 (1983), and Cohen P. Biochem. Soc. Trans. **(21)** 555-567 (1993)). The phosphorylation and dephosphorylation of GS are mediated by specific kinases and phosphatases. GSK-3 is responsible for phosphorylation and deactivation of GS, while glycogen bound protein phosphatase 1 (PP1G) dephosphorylates and activates GS. Insulin both inactivates GSK-3 and activates PP1G (Srivastava A K and Pandey S K Mol. and Cellular Biochem. **(182)** 135-141 (1998).

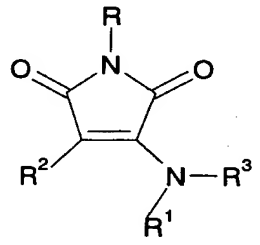
Chen et al Diabetes **(43)** 1234-1241 (1994) found that there was no difference in the mRNA abundance of PP1G between patients with Type II diabetes and control patients, suggesting that an increase in GSK-3 activity might be important in Type II diabetes. It has also recently been demonstrated that GSK-3 is overexpressed in Type II diabetic muscle and that an inverse correlation exists between skeletal muscle GSK-3α activity and insulin action (Nikoulina et al Glycogen Synthase Kinase-3 in Human Skeletal Muscle: Relationship To Insulin Resistance in Type II Diabetes Diabetes **(47(1))** 0028 Page A7 (1998) (Oral

presentation)). Additionally, in CHO cells, expressing both insulin receptor and insulin receptor substrate 1 (IRS-1), overexpression of GSK-3 resulted in an impairment of insulin action (Eldar-Finkelman and Krebs PNAS **(94)** 9660-9664 (1997)).

GSK-3 has been shown to phosphorylate other proteins in vitro, e.g. Tau protein, which is hyperphosphorylated in Alzheimer's disease, and the eukaryotic initiation factor eIF-2B at $Serine^{540}$. GSK-3 is known to be inhibited by lithium (Stambolic V., Ruel L.and Woodgett J.R. Curr. Biol. 1996 6(12): 1664-8) and lithium reduces the phosphorylation of tau, enhances the binding of tau to microtubules, and promotes microtubule assembly through direct and reversible inhibition of glycogen synthase kinase-3 (Hong M., Chen D.C., Klein P.S. and Lee V.M. J.Biol. Chem. 1997 272(40) 25326-32). WO 97/41854 (University of Pennsylvania) discloses that an effective drug for the treatment of manic depression is lithium, but that there are serious drawbacks associated with this treatment and the molecular mechanism underlying lithium's action for the treatment of manic depression has not been elucidated.

We have now discovered that certain substituted aminomaleimides are particularly potent and selective inhibitors of GSK-3. These compounds are therefore indicated to be useful for the treatment of conditions associated with a need for inhibition of GSK-3, such as diabetes, dementias, such as Alzheimer's disease, manic depression and cancer. Certain of these compounds are novel and such compounds comprise a further aspect of the invention.

Accordingly, in a first aspect the present invention provides a method for the treatment of conditions associated with a need for inhibition of GSK-3, such as diabetes, dementias, such as Alzheimer's disease, manic depression and cancer, which method comprises the administration of a pharmaceutically effective, non-toxic amount of a compound of formula (I):



(I)

or a pharmaceutically acceptable derivative thereof, wherein:
R is hydrogen, alkyl, aryl, or aralkyl;
R^1 is hydrogen, alkyl, aralkyl or alkoxyalkyl;
R^2 is substituted or unsubstituted aryl or substituted or unsubstituted heterocyclyl;

R^3 is hydrogen, alkyl, alkoxyalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl or aralkyl wherein the aryl moiety is substituted or unsubstituted; or

R^1 and R^3 together with the nitrogen to which they are attached form a single or fused, optionally substituted, saturated or unsaturated heterocylic ring, to a human or non-human mammal in need thereof.

Suitably, R is hydrogen.

Suitably, R^1 is hydrogen.

Suitably, R^2 is phenyl or naphthyl or substituted phenyl or substituted naphthyl, wherein substituents for the phenyl or naphthyl group are selected from up to three of C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkoxymethyl, halo, hydroxy, carboxy, cyano, nitro, C_{1-6}alkylthio, trifluoromethyl, trifluoromethyloxy, trifluoromethylthio, phenoxy, phenyl, benzyloxy and methylenedioxy.

Favourably, R^2 is phenyl either unsubstituted or substituted with up to three of methyl, methoxy, chloro or nitro.

Suitably, R^3 is phenyl either unsubstituted or substituted by up to three of C_{1-6}alkyl, phenyl, naphthyl, benzyl, C_{1-6}alkoxy, phenyloxy, phenylthio, carboxyC_{1-6}alkylthio carboxyphenylthio, benzyloxy, C_{1-6}alkylthio, halo, hydroxy, carboxy, cyano, nitro, acyl, hydroxymethyl, hydroxyethyl, trifluoromethyl, trifluoromethyloxy, trifluoromethylthio, trityl, carboxymethyl, cyanomethyl, carboxyC_{1-6}alkyloxy, C_{2-6} alkenyl, carboxyC_{2-6}alkenyl, carbamoyl, carbamoylC_{1-6}alkyl, C_{1-6}alkycarbonylamino, C_{1-6}alkylcarbonylalkylamino, C_{1-6}alkylaminosulphonylalkyl, mono- or bis-alkylphosphonateC_{1-6}alkyl, morpholinyl, adamantyl, oxazolyl and methylenedioxy or any two adjacent substituents on the phenyl ring together with the carbon atoms to which they are attached form a 5 or 6 membered carbocyclic ring or a 5 or 6 membered heterocyclic ring.

Favourably, R^3 is phenyl either unsubstituted or substituted with up to three of methyl, propyl, butyl, n-butoxy, phenoxy, thiomethyl, halo, hydroxy, benzyl, benzoyl, acetyl, 2-carboxyethenyl or any two adjacent substituents on the phenyl ring together with the carbon atoms to which they are attached form a fused cyclopentyl ring or a fused thiazolyl ring.

When R^1 and R^3 together with the nitrogen to which they are attached form a heterocylic ring, suitable rings include unsaturated rings having 5 to 8 ring atoms, such as imidazolyl.

When R^1 and R^3 together with the nitrogen to which they are attached form a heterocylic ring, suitable rings include saturated rings having 5 to 8 ring atoms, such as pyrrolidinyl, piperidinyl or azepinyl.

Suitable optional substituents for any heterocyclic ring represented by NR^1R^3 includes up to three of alkyl, hydroxy, nitro, carbamoyl, hydroxy(C_{1-4})alkyl or aryl(C_{1-4})alkyl or any two adjacent substituents of the ring, together with the carbon atoms to which they are attached, form a benzene ring.

There is a sub-group of compounds, falling wholly within formula (I), and being of formula (IA), wherein R, R^1, R^2 and R^3 are as defined in relation to formula (I), with the proviso that formula (IA) does not include:
3-indol-1-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
1-(1-methyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)pyridinium chloride;
1-[1-(4-methyl-pentyl)-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl]pyridinium chloride;
1-(1-dodecyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
3-[2-benzo[b]thien-2-yl-3-[4-(dimethylamino)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-carbamimidothioic acid,propyl ester;
3-(dimethylamino)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(methylamino)-1H-pyrrole-2,5-dione;
3-(1H-imidazo[4,5-b]pyridin-l-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-chloro-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-amino-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)- 1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1-piperidinyl)-1H-pyrrole-2,5-dione;
3-[4-(diphenylmethyl)-1-piperazinyl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
1-acetyl-3-[2,5-dihydro-1-methyl-2,5-dioxo-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrol-3-yl]- 1H-indole;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzotriazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-imidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione
3-(1H-indol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione
3-(1H-indazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[3-[(dimethylamino)methyl]-1H-indol-1-yl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)- 1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)- 1H-pyrrole-2,5-dione; and
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)- 1H-pyrrole-2,5-dione.

There is a further sub-group of compounds, falling wholly within formula (I), and being of formula (IB), wherein R, R^1, R^2 and R^3 are as defined in relation to formula (I), with the proviso that formula (IB) does not include:
3-phenylamino-4-phenyl-1H-pyrrole-2,5-dione;
3-phenyl-4-piperidin-1-yl-pyrrole-2,5-dione;
3-(4-methylpiperazin-l-yl)-4-phenyl-pyrrole-2,5-dione;
3-(4-ethylpiperazin-l-yl)-4-phenyl-pyrrole-2,5-dione;
3-(4-chlorophenyl)-4-(4-methyl-piperazin-l-yl)-pyrrole-2,5-dione;
3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-morpholin-4-yl-pyrrole-2,5-dione;
3-indol-1-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
1,3-dimethyl-4-methylaminopyrrole-2,5-dione;
1-(1-methyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-1-(4-methyl-pentyl)-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
1-(1-dodecyl-2,5-dioxo-4-phenylamino-2,5-dihydro-1H-pyrrol-3-yl)-pyridinium chloride;
3-[2,5-dihydro-4-(1H-imidazol-1-yl)-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]-1H-indole-1-carboxylic acid, 1,1-dimethylethyl ester;
3-[2-benzo[b]thien-2-yl-3-[4-(dimethylamino)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]-1H-indol-1-yl]-carbamimidothioic acid,propyl ester;
3-(dimethylamino)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(phenylamino)-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(methylamino)-1H-pyrrole-2,5-dione;
3-(1H-imidazo[4,5-b]pyridin-l-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-chloro-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(6-amino-9H-purin-9-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)- 1H-pyrrole-2,5-dione;
3-(1H-indol-3-yl)-1-methyl-4-(1-piperidinyl)-1H-pyrrole-2,5-dione;
3-[4-(diphenylmethyl)-1-piperazinyl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;

1-acetyl-3-[2,5-dihydro-1-methyl-2,5-dioxo-4-[[4-(trifluoromethyl)phenyl]amino]-1H-pyrrol-3-yl]- 1H-indole;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-benzotriazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-imidazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione
3-(1H-indol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione
3-(1H-indazol-1-yl)-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-[3-[(dimethylamino)methyl]-1H-indol-1-yl]-4-(1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)- 1H-pyrrole-2,5-dione;
3-(1H-benzimidazol-1-yl)-4-(1H-indol-3-yl)- 1H-pyrrole-2,5-dione;
3-(1H-indol-1-yl)-4-(1-methyl-1H-indol-3-yl)- 1H-pyrrole-2,5-dione;
3,3'-iminobis[1-methyl-4-(4-methylphenyl)- 1H-pyrrole-2,5-dione;
1-[4-(2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-2,5-dihydro-2,5-dioxo-1H-pyrrol-3-yl]pyridinium internal salt;
1-[4-(2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-2,5-dihydro-1-methyl-2,5-dioxo-1H-pyrrol-3-yl]pyridinium internal salt; and
3-(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)-4-(4-morpholinyl)-1H-pyrrole-2,5-dione.

It is considered that the compounds of formula (IB) are novel. Accordingly , the present invention also provides a compound of the above defined formula (IB) or a derivative thereof.

Certain of the compounds of formula (I) may contain at least one chiral carbon, and hence they may exist in one or more stereoisomeric forms. The present invention encompasses all of the isomeric forms of the compounds of formula (I) whether as individual isomers or as mixtures of isomers, including racemates.

Alkyl groups referred to herein, including those forming part of other groups, include straight or branched chain alkyl groups containing up to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups selected from the list consisting of aryl, heterocyclyl, alkylthio, alkenylthio, alkynylthio, arylthio, heterocyclylthio, alkoxy, arylalkoxy, arylalkylthio, amino, mono- or di-alkylamino, cycloalkyl, cycloalkenyl, carboxy and esters thereof, hydroxy, and halogen.

Alkenyl and alkynyl groups referred to herein include straight and branched chain alkenyl groups containing from two to six carbon atoms, said carbon atoms being optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

Cycloalkyl and cycloalkenyl groups referred to herein include groups having between three and eight ring carbon atoms, which carbon atoms are optionally substituted with up to five, suitably up to three, groups including those substituents described hereinbefore for the alkyl group.

When used herein the term "aryl" includes phenyl and biphenyl groups, for example naphthyl, especially phenyl.

Suitably optional substituents for any aryl group include up to three substituents selected from the list consisting of halo, alkyl, alkenyl, substituted alkenyl, arylalkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkyloxy, hydroxy, hydroxyalkyl, nitro, amino, cyano, cyanoalkyl , mono- and di-N-alkylamino, acyl, acylamino, N-alkylacylamino, acyloxy, carboxy, carboxyalkyl, carboxyalkylcarbonyl, carboxyalkenyl, ketoalkylester, carbamoyl, carbamoylalkyl, mono- and di-N-alkylcarbamoyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy, arylthio, aralkyloxy, aryloxycarbonyl, ureido, guanidino, morpholino, adamantyl, oxazolyl, aminosulphonyl, alkylaminosulphonyl, alkylthio, haloalkylthio, alkylsulphinyl, alkylsulphonyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, trityl, substituted trityl, mono- or bis-alkylphosphonate or mono- or bis-alkylphosphonateC_{1-6}alkyl or any two adjacent substituents on the phenyl ring together with the carbon atoms to which they are attached form a carbocyclic ring or a heterocyclic ring.

When used herein the terms "heterocyclyl" and "heterocyclic" suitably include, unless otherwise defined, aromatic and non-aromatic, single and fused, rings suitably containing up to four heteroatoms in each ring, each of which is selected from oxygen, nitrogen and sulphur, which rings, may be unsubstituted or substituted by, for example, up to three substituents. Each ring suitably has from 4 to 7, preferably 5 or 6, ring atoms. A fused heterocyclic ring system may include carbocyclic rings and need include only one heterocyclic ring.

Substituents for any heterocyclyl or heterocyclic group are suitably selected from halogen, alkyl, arylalkyl, alkoxy, alkoxyalkyl, haloalkyl, hydroxy, amino, mono- and di-N-alkyl-amino, acylamino, carboxy salts, carboxy esters, carbamoyl, mono- and di-N-alkylcarbonyl, aryloxycarbonyl, alkoxycarbonylalkyl, aryl, oxy groups, ureido, guanidino, sulphonylamino, aminosulphonyl, alkylthio, alkylsulphinyl, alkylsulphonyl, heterocyclyl and heterocyclylalkyl.

When used herein 'halo' includes iodo, bromo, chloro or fluoro, especially chloro or fluoro.

Suitable derivatives of the compounds of the invention are pharmaceutically acceptable derivatives.

Suitable derivatives of the compounds of the invention include salts and solvates.

Suitable pharmaceutically acceptable derivatives include pharmaceutically acceptable salts and pharmaceutically acceptable solvates.

Suitable pharmaceutically acceptable salts include metal salts, such as for example aluminium, alkali metal salts such as lithium, sodium or potassium, alkaline earth metal salts such as calcium or magnesium and ammonium or substituted ammonium salts, for example those with lower alkylamines such as triethylamine, hydroxy alkylamines such as 2-hydroxyethylamine, bis-(2-hydroxyethyl)-amine or tri-(2-hydroxyethyl)-amine, cycloalkylamines such as bicyclohexylamine, or with procaine, dibenzylpiperidine, N-benzyl-b-phenethylamine, dehydroabietylamine, N,N'-bisdehydroabietylamine, glucamine, N-methylglucamine or bases of the pyridine type such as pyridine, collidine, quinine or quinoline.

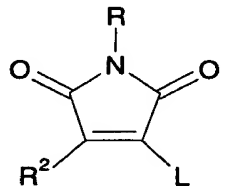
Suitable pharmaceutically acceptable salts also includes pharmaceutically acceptable acid addition salts, such as those provided by pharmaceutically acceptable inorganic acids or organic acids.

Suitable pharmaceutically acceptable acid addition salts provided by pharmaceutically acceptable inorganic acids includes the sulphate, nitrate, phosphate, borate, hydrochloride and hydrobromide and hydroiodide.

Suitable pharmaceutically acceptable acid addition salts provided by pharmaceutically acceptable organic acids includes the acetate, tartrate, maleate, fumarate, malonate, citrate, succinate, lactate, oxalate, benzoate, ascorbate, methanesulphonate, a-keto glutarate and a-glycerophosphate.

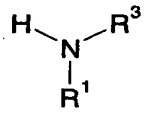
Suitable pharmaceutically acceptable solvates include hydrates.

A further aspect of the invention provides a process for the preparation of a compound of the invention, which process comprises reaction of a compound of formula (II):



(II)

wherein R and R^2 are as defined in formula (I) and L is a leaving group, with a compound of formula (III):



(III)

wherein R^1 and R^3 are as defined in formula (I); and thereafter, if required, carrying out one or more of the following optional steps:

(i) converting a compound of formula (I) to a further compound of formula (I);

(ii) removing any necessary protecting group;

(iii) preparing an appropriate derivative of the compound so formed.

Examples of suitable leaving groups, L, are chloro and hydroxy.

The reaction between the compounds of formulae (II) and (III) is carried out in any suitable solvent, for example 1-methyl-2-pyrrolidinone or methanol, under conventional amination conditions at any temperature providing a suitable rate of formation of the required product, generally an elevated temperature, over a suitable reaction time.

Suitable reaction temperatures include those in the range of 60°C to 220°C and, as appropriate, the reflux temperature of the solvent. Temperatures at the upper end of this range are preferentially employed when the compound of formula (III) is a weak nucleophile. Conventional methods of heating also include the use of microwave heating devices, for example a microwave reactor, such as a 100 watt reactor.

The reaction products are isolated using conventional methods. Typically, the reaction mixture is cooled, the residue acidified and the products extracted using solvent extraction, suitably using an organic solvent.

The reaction products are purified by conventional methods, such as chromatography and trituration.

Crystalline product may be obtained by standard methods.

In a preferred aspect, a solution of the compound of formula (II) and a compound of formula (III) in methanol is heated to reflux from between 1 to 4 days, then cooled and concentrated. The residue is then acidified with hydrochloric acid, and extracted with ethyl acetate. The organic extracts are then washed with water, brine, dried with anhydrous magnesium sulphate, and the solvent is removed. The product is then purified by standard methods such as trituration or chromatography, on silica gel, to afford the desired compound.

The above mentioned conversion of a compound of formula (I) into another compound formula (I) includes any conversion which may be effected using conventional procedures, but in particular the said conversions include any combination of:

(i) converting one group R into another group R;

(ii) converting one group R_{10} into another group R_{10}; and

(iii) converting one group R_{11} into another group R_{11}.

The above mentioned conversions (i) to (iii) may be carried out using any appropriate method under conditions determined by the particular groups chosen: Thus, suitable conversions of one group R into another group R, as in conversion (i), include:

(a) converting a group R which represents hydrogen into a group R which represents an alkyl or arylalkyl group; such conversion may be carried out using an appropriate conventional alkylation procedure, for example treating an appropriately protected compound of formula (I) with an alkylating agent; and

(b) converting a group R which represents an alkyl group into a group R where R represents hydrogen; such conversion may be carried out using an appropriate dealkylation procedure, for example treating an appropriately protected compound of formula (I) with aqueous base followed by ammonium hydroxide.

Suitable conversions of one group R_{10} into another group R_{10}, as in conversion (ii), include:

(a) converting a group R_{10} which represents nitro into a group R_{10} which represents amino, such conversion may be carried out using a conventional reduction procedure, for example hydrogenating an appropriately protected compound of formula (I);

(b) converting a group R_{10} which represents nitro into a group R_{10} which represents acetylamino, such conversion may be carried out using an appropriate conventional reductive acylation procedure, for example hydrogenating an appropriately protected compound of formula (I) followed by acylation of the resultant amino group with an acylating agent;

(c) converting a group R_{10} which represents amino into a group R_{10} which represents substituted aminocarbonyl, such conversion may be carried out using an appropriate conventional amidation procedure, for example treating an appropriately protected compound of formula (I) with an appropriately substituted isocyanate;

(d) converting a group R_{10} which represents amino into a group R_{10} which represents acylamino, such conversion may be carried out using an appropriate conventional acylation procedure, for example treating an appropriately protected compound of formula (I) with an acylating agent; and

(e) converting a group R_{10} which represents iodo into a group R_{10} which represents alkoxycarbonyl, such conversion may be carried out using an appropriate procedure, for example treating an appropriately protected compound of formula (I) with carbon monoxide and methanol in the presence of a palladium (0) complex.

Suitable conversions of one group R_{11} into another group R_{11}, as in conversion (iii), include:

(a) converting a group R_{11} which represents a t-BOC-protected amino group into a group R_{11} which represents amino, such conversion may be carried out using an appropriate conventional deprotection procedure, for example deprotecting a t-BOC-protected compound of formula (I) with trifluoroacetic acid;

(b) converting a group R_{11} which represents a carboxylic acid group into a group R_{11} which represents an amide group, such conversion may be carried out using an appropriate conventional procedure, for example treating an appropriately protected compound of formula (I) with an amine in the presence of a suitable activating agent such as 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide; and

(c) converting a group R_{11} which represents alkoxy into a group R_{11} which represents amino, such conversion may be carried out using an appropriate conventional procedure, for example treating an appropriately protected compound of formula (I) with methanolic ammonia solution followed by aqueous ammonia.

The above mentioned conversions may as appropriate be carried out on any of the intermediate compounds mentioned herein.

Suitable protecting groups in any of the above mentioned reactions are those used conventionally in the art The methods of formation and removal of such protecting groups are those conventional methods appropriate to the molecule being protected. Thus for example a benzyloxy group may be prepared by treatment of the appropriate compound with a benzyl halide, such as benzyl bromide, and thereafter, if required, the benzyl group may be conveniently removed using catalytic hydrogenation or a mild ether cleavage reagent such as trimethylsilyl iodide or boron tribromide.

Where appropriate individual isomeric forms of the compounds of formula (I) may be prepared as individual isomers using conventional chemical procedures.

The absolute stereochemistry of compounds may be determined using conventional methods, such as X-ray crystallography.

The derivatives of the compounds of formula (I), including salts and/or solvates, may be prepared and isolated according to conventional procedures.

The compounds of formula (II) are known compounds or they may be prepared using methods analogous to those used to prepare such compounds such as those described in International Patent Application, Publication Number WO97/34890 and Wiley, R.H. and Slaymaker, S.C. J. Am. Chem. Soc. (80) 1385

(1958). The compounds of formula (II) may be inter-converted in an analogous manner to the above mentioned inter-conversions of the compounds of formula (I).

The compounds of formula (III) are known commercially available compounds or they may be prepared using methods analogous to those used to prepare known compounds, for example those disclosed in standard reference texts of synthetic methodology such as J. March, Advanced Organic Chemistry, 3rd Edition (1985), Wiley Interscience.

As stated above, the compounds of formula (I), or pharmaceutically acceptable derivatives thereof, are indicated to be useful as inhibitors of glycogen synthase kinase-3.

Thus the present invention further provides a compound of formula (I), or a pharmaceutically acceptable derivative thereof, for use as an inhibitor of glycogen synthase kinase-3, and especially for use in the treatment of conditions associated with a need for the inhibition of glycogen synthase kinase-3, such as diabetes, dementias, such as Alzheimer's disease, manic depression and cancer.

The present invention also provides the use of a compound of formula (I), or a pharmaceutically acceptable derivative thereof, for the manufacture of a medicament for the treatment of conditions associated with a need for the inhibition of glycogen synthase kinase-3, such as diabetes, dementias, such as Alzheimer's disease, manic depression and cancer.

As indicated above, formula (I) comprises a sub-group of compounds of formula (IA). In a further aspect of this invention, there is provided a compound of formula (IA), or a pharmaceutically acceptable derivative thereof, for use as an active therapeutic substance.

Accordingly, the invention also provides a pharmaceutical composition which comprises a compound of formula (IA), or a pharmaceutically acceptable derivative thereof, and a pharmaceutically acceptable carrier.

Preferably, the compounds of formula (I), or pharmaceutically acceptable derivatives thereof are administered as pharmaceutically acceptable compositions.

The compositions of the invention are preferably adapted for oral administration. However, they may be adapted for other modes of administration.

The compositions may be in the form of tablets, capsules, powders, granules, lozenges, suppositories, reconstitutable powders, or liquid preparations, such as oral or sterile parenteral solutions or suspensions.
In order to obtain consistency of administration it is preferred that a composition of the invention is in the form of a unit dose.

Preferably the composition are in unit dosage form. A unit dose will generally contain from 0.1 to 1000 mg of the active compound.

Generally an effective administered amount of a compound of the invention will depend on the relative efficacy of the compound chosen, the severity of the disorder being treated and the weight of the sufferer. However, active compounds will typically be administered once or more times a day for example 2, 3 or 4 times daily, with typical total daily doses in the range of from 0.1 to 800 mg/kg/day.

Suitable dose forms for oral administration may be tablets and capsules and may contain conventional excipients such as binding agents, for example syrup, acacia, gelatin, sorbitol, tragacanth, or polyvinylpyrrolidone; fillers, for example lactose, sugar, maize-starch, calcium phosphate, sorbitol or glycine; tabletting lubricants, for example magnesium stearate; disintegrants, for example starch, polyvinylpyrrolidone, sodium starch glycollate or microcrystalline cellulose; or pharmaceutically acceptable wetting agents such as sodium lauryl sulphate.

The solid oral compositions may be prepared by conventional methods of blending, filling or tabletting. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are of course conventional in the art. The tablets may be coated according to methods well known in normal pharmaceutical practice, in particular with an enteric coating.

Oral liquid preparations may be in the form of, for example, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethylcellulose, aluminium stearate gel, hydrogenated edible fats; emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example almond oil, fractionated coconut oil, oily esters such as esters of glycerine, propylene glycol, or ethyl alcohol; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid; and if desired conventional flavouring or colouring agents.

For parenteral administration, fluid unit dosage forms are prepared utilizing the compound and a sterile vehicle, and, depending on the concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions the compound can be dissolved in water for injection and filter sterilized before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, a preservative and buffering agents can be dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are

prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilization cannot be accomplished by filtration. The compound can be sterilized by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

GSK-3 Assays

Types of GSK-3 assay used to test the compounds of the invention include the following:

Type 1: The GSK-3 specific peptide used in this assay was derived from the phosphorylation site of glycogen synthase and its sequence is: YRRAAVPPSPSLSRHSSPHQ(S)EDEEE. (S) is pre-phosphorylated as is glycogen synthase in vivo and the three consensus sites for GSK-3 specific phosphorylation are underlined. The buffer used to make up the glycogen synthase peptide and [γ-^{33}P] ATP consisted of MOPS 25mM, EDTA 0.2mM, MgAcetate 10mM, Tween-20 0.01% and mercaptoethanol 7.5mM at pH 7.00.

The compounds were dissolved in dimethyl sulphoxide (DMSO) to a final concentration of 100mM. Various concentrations were made up in DMSO and mixed with the substrate (GSK-3 peptide) solution (to a final concentration 20uM) described in the above section along with rabbit or human GSK-3α and GSK-3β (final concentration 0.5U/ml enzyme). The reactions were initiated with the addition of [γ-^{33}P] ATP (500cpm/pmole) spiked into a mixture of ATP (final concentration of 10μM). After 30 min at room temperature the reaction was terminated by the addition of 10μl of H_3PO_4 / 0.01% Tween-20 (2.5%). A volume (10μl) of the mixture was spotted onto P-30 phosphocellulose paper (Wallac & Berthold, EG&G Instruments Ltd, Milton Keynes). The paper was washed four times in H_3PO_4 (0.5%), 2 mins for each wash, air dried and the radioactive phosphate incorporated into the synthetic glycogen synthase peptide, which binds to the P-30 phosphocellulose paper, was counted in a Wallac microbeta scintillation counter.

Analysis of Data: Values for IC50 for each inhibitor were calculated by fitting a four-parameter logistic curve to the model : cpm=lower+(upper-lower) /(1 + (concentration/ IC50) ^{slope}).

Type 2: This protocol is based on the ability of the kinase to phosphorylate a biotinylated 26 mer peptide, sequence of which derived from the phosphorylation site of glycogen synthase and its sequence is Biot-

YRRAAVPPSPSLSRHSSPHQ(S)EDEEE, with (S) is a pre-phosphorylated serine as is glycogen synthase in vivo and the three consensus sites for GSK-3 specific phosphorylation are underlined. The phosphorylated biotinylated peptide is then captured onto streptavidin coated SPA beads (Amersham Technology), where the signal from the 33P is amplified via the scintillant contained in the beads.

The kinase was assayed at a concentration of 10 nM final in 25 mM MOPS buffer, pH 7.0 containing 0.01% Tween-20, 7.5 mM 2-mercaptoethanol, 10 mM Magnesium acetate, and 10 uM [γ-^{33}P]-ATP. After 60 minutes incubation at room temperature, the reaction was stopped by addition of 50 mM EDTA solution containing the Streptavidin coated SPA beads to give a final 0.5 mgs of beads per assay well in a 384 microtiter plate format.

10 mM stock solutions of the compounds of the invention in 100% DMSO are generated as a first step in the screening process. The second step involves the creation of dose response plates where these compounds are diluted across the plate where the final low and high concentrations are to be 0.008 and 10 uM final in the kinase assay. The third step involves the creation of the assay plates. This is achieved by transferring the compounds from four 96 dose response plates to one 384 assay plate on the Robocon Robolab system. The fourth step is to perform the assay as described and count the resulting plates in the Trilux (Wallac 1450 microbeta liquid scintillation and luminescence counter). The final step is data acquisition and analysis where IC_{50} values are generated for each compound in duplicate by fitting a four parameter logistic curve to the model : cpm = lower + (upper-lower) / (1 + (concentration / IC_{50}) ^{slope}) in a batch manner.

The most potent compounds of the present invention show IC50 values in the range of from between 10 to 100 nM.

No adverse toxicological effects are expected for the compounds of the invention, when administered in accordance with the invention.

The following Examples illustrate the invention, but do not limit it in any way.

Example 1

3-(3-Bromophenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A solution of 3-bromoaniline (2.27 mL, 0.020 mol) and 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (2.02 g, 0.0083 mol; prepared by analogy with the methods described in WO97/34890 and Wiley, R.H. and Slaymaker, S.C. J. Am. Chem. Soc. (80) 1385 (1958)) in methanol (50 mL) was heated at reflux for 40 hours, cooled and concentrated. The residue was acidified with aqueous hydrochloric acid (1M, 200 mL) and extracted with ethyl acetate (3 x 200 mL). The combined organic solutions were washed with water and brine, dried with magnesium sulphate, evaporated and the residue chromatographed on silica gel using dichloromethane-diethyl ether (gradient from 100:0 to 95:5 v/v) as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.70-7.30 (8H, m), δ9.65 (1H, br), δ10.90 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 377/379/381 ($C_{16}H_{10}BrClN_2O_2$ requires $[M+H]^+$ at m/z 377/379/381).

Example 2

3-(4-Benzoylphenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A sealed tube (comprising threaded glass tube with resealable cap) containing a mixture of 4-aminobenzophenone (0.147 g, 0.75 mmol), 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (0.061 g, 0.25 mmol) and 1-methyl-2-pyrrolidinone (0.5 mL) was irradiated in a microwave reactor for 12 minutes at 100 Watts. The mixture was diluted with aqueous hydrochloric acid (5 mL) and extracted with ethyl acetate (2 x 5 mL). The combined organic solutions were evaporated and the residue chromatographed on silica gel using dichloromethane as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.85 (2H, d), δ7.00 (2H, d), δ7.25 (2H, d), δ7.35 (2H, d), δ7.50-7.70 (5H, m), δ9.95 (1H, s), δ10.95 (1H, s)
MS (APCI -ve): $[M]^-$. at m/z 402/404 ($C_{23}H_{15}ClN_2O_3$ requires $[M]^-$. at m/z 402/404)

Example 3

3-(3-Bromo-4-methylphenylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione

A mixture of 3-bromo-4-methylaniline (0.220 g, 1.18 mmol), 3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (0.100 g, 0.40 mmol) and 1-methyl-2-pyrrolidinone (1.0 mL) was heated in an oil bath at 200°C for 51 minutes. The

mixture was diluted with aqueous hydrochloric acid (5 mL) and extracted with ethyl acetate (5 mL). The combined organic solutions were evaporated and the residue chromatographed on silica gel using dichloromethane as eluent to afford the title compound, a solid, following trituration with dichloromethane-hexane (90:10 v/v).

^{1}H NMR ($CDCl_3$): δ2.24 (3H, s), δ6.65-7.70 (7H, m, reduces to 5H on D_2O exchange) and δ8.05 (2H, m).
MS (APCI -ve): $[M-H]^-$ at m/z 400/402 ($C_{17}H_{12}BrN_3O_4$ requires $[M-H]^-$ at m/z 400/402).

Example 4
3-(4-Methylphenylamino)-4-(4-hydroxyphenyl)-1H-pyrrole-2,5-dione
A mixture of 3-hydroxy-4-(4-hydroxyphenyl)-1H-pyrrole-2,5-dione (103 mg, 0.5 mmol) and 4-methylaniline (59 mg, 0.55 mmol) in 1-methyl-2-pyrrolidinone (1mL) was heated in a sealed tube at 150°C for 24hours. The reaction mixture was dissolved in ethyl acetate(20 mL) and washed with 1N HCl (2 x 20 mL), water (3 x 20 mL) and brine (20 mL). The solution was dried over magnesium sulphate, evaporated and the residue chromatographed on silica gel using dichloromethane-diethyl ether (gradient from 100:0 to 90:10 v/v) as eluent to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ2.35 (3H, s), δ6.50 (2H, d), δ6.64 (2H, d), δ6.77 (2H, d), δ6.90 (2H, d), δ9.26 (1H, br), δ9.44 (1H, br), δ10.64 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 295 ($C_{17}H_{14}N_2O_3$ requires $[M+H]^+$ at m/z 295).

Example 5
3-(N-Methyl-N-phenylamino)-4-(indol-3-yl)-1H-pyrrole-2,5-dione.
A mixture of 3-(N-methyl-N-phenylamino)-4-(indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione (Table B, Example B1; 2.00 g, 0.006 mol), aqueous potassium hydroxide solution (10% w/v, 2 L), ethanol (50 mL) and *n*-butanol (200 mL) was heated at reflux for 5 hours. The cooled reaction mixture was filtered and the filtrate acidified to pH 1 by addition of conc. hydrochloric acid. The mixture was cooled to 0°C and the resulting solid filtered, washed with water and recrystallised from acetonitrile to give the corresponding maleic anhydride. This anhydride (0.4 g, 1.25 mmol) was suspended in a mixture of concentrated aqueous ammonium hydroxide and DMF and heated in stainless steel bomb at 130°C for 4

hours. The resulting mixture was diluted with water and extracted with dichloromethane and the dried organic solution evaporated to give a solid. This was chromatographed on silica gel using a gradient of 0-5% (v/v) of methanol in dichloromethane as eluent to afford the title compound, a solid.

^{1}H NMR (DMSO-d_6): δ3.07 (3H, s), δ6.75-7.45 (9H, m), δ7.68 (1H, s), δ10.70 (1H, br) and δ11.70 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 318 ($C_{19}H_{15}N_3O_2$ requires $[M+H]^+$ at m/z 318).

Further elution of the chromatography column afforded 3-amino-4-(indol-3-yl)-1H-pyrrole-2,5-dione (Table B, Example B2) as a byproduct.

Example 6
3-(Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione
3-(Indan-5-ylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Table A, Example A359; 0.3 g, 0.9 mmol) and 10% Pd/C (60 mg) in ethanol (25 mL) was hydrogenated at atmospheric temperature and pressure for 2 hours. The reaction mixture was filtered through Kieselguhr and the filtrate concentrated in vacuo to give an orange solid. The crude product was taken up in dichloromethane (10 mL) and treated with di-tert-butyl dicarbonate (0.216 g, 1 mmol) and the mixture stirred at ambient temperature for 18 hours. The reaction mixture was poured into saturated aqueous sodium bicarbonate (10 mL) and extracted into dichloromethane (3x10 mL). The combined organics were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography on silica gel using dichloromethane-methanol gave the product *amine* as an orange powder.

^{1}H NMR (DMSO-d_6): δ1.85 (2H, quintet), δ2.50 (2H, t), δ2.66 (2H, t), δ4.82 (2H, s), δ5.89 (1H, d), δ6.36 (2H, m), δ6.47 (1H, s), δ6.25 (2H, m), δ6.85 (1H, d), δ9.13 (1H, br) and δ10.58 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 320 ($C_{19}H_{17}N_3O_2$ requires $[M+H]^+$ at m/z 320)

Example 7
3-(Indan-5-ylamino)-4-(3-acetylaminophenyl)-1H-pyrrole-2,5-dione
3-(Indan-5-ylamino)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Table A, Example A359; 0.3 g, 0.9 mmol) and 10% Pd/C (60 mg) in ethanol (25 mL) was

hydrogenated at atmospheric temperature and pressure for 2 hours. The reaction mixture was filtered through Kieselguhr and the filtrate concentrated in vacuo to give an orange solid. The crude product was taken up in dichloromethane (5 mL) and treated with acetic anhydride (85 µL, 0.9 mmol) and stirred for 3 hours at ambient temperature. The reaction mixture was poured onto saturated aqueous sodium bicarbonate solution (10 mL) and extracted into ethyl acetate (3x10 mL). The combined organics were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. Chromatography on silica gel using dichloromethane-methanol gave the desired compound as an orange powder.

^{1}H NMR (DMSO-d_6): δ1.83(2H, quintet), δ2.02 (3H, s), δ2.45 (2H, t), δ2.66 (2H, t), δ6.41 (2H, m), δ6.59 (1H, d), δ6.84 (2H, d), δ6.90 (1H, t), δ7.38 (1H, d), δ9.30 (1H, bs), δ9.68 (1H, s) and δ10.61 (1H, bs)]
MS (APCI –ve): $[M-H]^-$ at m/z 360 ($C_{21}H_{19}N_3O_3$ requires $[M-H]^-$ at m/z 360).

Example 8
3-(Indan-5-ylamino)-4-[3-[(3-fluorophenylaminocarbonyl)amino]phenyl]-1H-pyrrole-2,5-dione
3-(Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione (Table A, Example A599; 0.08 g, 0.3 mmol) in dichloromethane (10 mL) was was treated with 3-fluorophenyl isocyanate (0.038mg, 0.3 mmol). The mixture was shaken on an orbital shaker for 72 hours. Saturated aqueous sodium bicarbonate (5 mL) was added, shaking continued for 5 minutes and the organic layer transferred directly onto a column of silica gel. Elution with dichloromethane gave the product as a yellow solid.

^{1}H NMR (DMSO-d_6): δ1.78 (2H, quintet), δ2.44 (2H, t), δ2.62 (2H, t), δ6.47 (2H, m), δ6.61 (1H, dd), δ6.83 (2H, m), δ6.93 (2H, m), δ7.09 (1H, dd), δ7.28 (2H, m), δ7.45 (1H, dd), δ8.42 (1H, br), δ8.72 (1H, br), δ9.30 (1H, br) and δ10.65 (1H, br).
MS (APCI -ve) $[M]^-$ at m/z 456 ($C_{26}H_{21}FN_4O_3$ requires $[M]^-$ at m/z 456).

Example 9
3-(Indan-5-ylamino)-4-[3-(benzoylamino)phenyl]-1H-pyrrole-2,5-dione
3-(5-Indan-5-ylamino)-4-(3-aminophenyl)-1H-pyrrole-2,5-dione (Table A, Example A599; 0.100 g, 0.3 mmol) in dichloromethane (3 mL) was added to a solution of benzoic acid (0.042 g, 0.33 mmol), 1-hydroxybenzotriazole (0.047 g, 0.33 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

(0.063 g, 0.33 mmol in dichloromethane (5 mL). The mixture was shaken on an orbital shaker for 72 hours. Saturated aqueous sodium bicarbonate (5 mL) was added, shaking continued for 5 minutes and the organic layer transferred directly onto a column of silica gel. Elution with dichloromethane gave the product as a yellow solid.

^{1}H NMR (DMSO-d_6): δ1.83 (2H, quintet), δ2.43 (2H, t), δ2.57 (2H, t), δ6.42 (1H, s), δ6.30 (2H, m), δ6.83 (1H, d), δ7.02 (1H, t), δ7.22 (1H, s), δ7.56 (4H, m), δ7.86 (2H, dd), δ9.38 (1H, br), δ9.98 (1H, br) and δ10.68 (1H, bs).
MS (APCI –ve): $[M-H]^-$ at m/z 422 ($C_{26}H_{21}N_3O_3$ requires $[M-H]^-$ at m/z 422)

Example 10
3-[4-(2-Aminoethyl)phenylamino]-4-(2-methoxyphenyl)-1H-pyrrole-2,5-dione
A solution of 3-[4-[2-(*t*-butoxycarbonylamino)ethyl]phenylamino]-4-(2-methoxyphenyl)-1H-pyrrole-2,5-dione (0.060 g, 0.13 mmol) and trifluoroacetic acid (4 drops) in dry DCM (5 mL) was stirred for 18 hours at room temperature. The suspension was diluted with ethyl acetate (10 mL), poured onto sodium bicarbonate (20 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic solutions were washed with brine, dried with magnesium sulfate, evaporated and the residue triturated with a mixture of hexane-dichloromethane (95:5 v/v) to afford the title compound as an orange solid.

^{1}H NMR ($CDCl_3$); δ1.52 (2H, br), δ2.59 (2H, t), δ2.83 (2H, t), δ3.16 (3H, s), δ6.44 (1H, d), δ6.58 (2H, d), δ6.79 (2H,d), δ6.97-6.93 (1H, m), δ7.22-7.17 (3H, m) and δ7.33 (1h, d).
MS (APCI +ve): $[M+H]^+$ at m/z 338 ($C_{19}H_{19}N_3O_3$ requires $[M+H]^+$ at 338).

Example 11
3-(3-Fluoro-4-methylphenylamino)-4-[4-(methoxycarbonyl)phenyl]-1H-pyrrole-2,5-dione
A mixture of 3-(3-Fluoro-4-methylphenyl-amino)-4-(4-iodophenyl)-1H-pyrrole-2,5-dione (Example A705, 126 mg, 0.3 mmol), tetrakis(triphenyl phosphine)-palladium(0) (35 mg, 0.03 mmol) and methanol (10 mL) was placed in a 50mL two necked round bottomed flask. One arm of the flask was sealed with a septum and to the other arm was fitted a reflux condenser, topped with a multiway tap connected respectively to vacuum, a carbon monoxide cylinder and to a balloon. Using the multiway tap, the flask was alternately evacuated and flushed with carbon monoxide, and the process repeated several times to unsure an atmosphere

of carbon monoxide within the flask. The balloon was charged with carbon monoxide and this was then opened to the reaction flask for the duration of the reaction in order to maintain a slight positive pressure of carbon monoxide within the flask. Triethylamine (100 uL, 0.7 mmol) was added and the mixture heated at reflux for 16 hours. The mixture was cooled and diluted with ethyl acetate and the resulting solution washed with aqueous hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The organic solution was dried over magnesium sulphate and evaporated to afford a solid. This was chromatographed on silica gel using dichloromethane-ether (98:2 v/v) as eluent to afford the title compound, a solid.

^{1}H NMR ($CDCl_3$); δ2.14 (3H, s), δ3.90 (3H, s), δ6.35-7.30 (7H, m) and δ7.82 (2H, m).
MS (APCI +ve): $[M+H]^+$ at m/z 355 ($C_{19}H_{15}FN_2O_4$ requires $[M+H]^+$ at 355).

Example 12
3-[4-[2-[N-[6-(Acetylamino)hexyl]aminocarbonyl]ethyl]phenylamino]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione
A solution of triethylamine (81 mg, 0.8 mmol) in dry N, N-dimethylformamide (5 mL) was added to a mixture of 3-[4-[2-(hydroxycarbonyl)ethyl]phenylamino]-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Example A763, 152 mg, 0.4 mmol), N-(6-aminohexyl)acetamide hydrochloride (78 mg, 0.4 mmol), 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (77 mg, 0.4 mmol) and 1-hydroxybenzotriazole (54 mg, 0.4 mmol) and the resulting mixture stirred at room temperature for 18 hours. The mixture was diluted with ethyl acetate (25 mL) and washed successively with water (2 x 25 mL), saturated aqueous sodium bicarbonate solution (25 mL), water (2 x 25 mL), brine (25 mL), dried over magnesium sulphate and concentrated. The residue was redissolved in dichloromethane-methanol (1:1 v/v), filtered and evaporated to afford the title compound as a foam.

^{1}H NMR (DMSO-d_6); δ1.10-1.40 (8H, m), δ1.77 (3H, s), δ2.15 (2H, m), δ2.55 (2H, m), δ3.00 (4H, m), δ6.62 (2H, d), δ6.77 (2H, d), δ7.20-7.90 (6H, m), δ9.80 (1H, br) and δ10.85 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 522 ($C_{27}H_{31}N_5O_6$ requires $[M+H]^+$ at 522).

Example 13
3-[4-(*trans*-2-carboxyethenyl)phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione

A mixture of *trans*-4-aminocinnamic acid (0.205 g, 1.26 mmol), 3-chloro-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (0.123 g, 0.51 mmol) and 1-methyl-2-pyrrolidinone (1.0 mL) was heated in a sealed tube in a hotblock set at 69°C for 28.5 hours. The mixture was diluted with aqueous hydrochloric acid (10 mL) and extracted with ethyl acetate (2x20 mL). The combined organics were washed with brine (2x10 mL), dried over anhydrous magnesium sulphate and evaporated to dryness. The residue was triturated with a mixture of dichloromethane and ethyl acetate to afford the title compound as a solid.

^{1}H NMR (DMSO-d_6): δ6.35 (1H, d), 6.74 (2H, d), 6.99 (2H, d), 7.19(2H, d), 7.35 (2H, d), 7.42 (1H, d), 9.76 (1H, br), 10.89(1H, br) and δ12.23 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 369/371 ($C_{19}H_{13}N_2O_4$ requires $[M+H]^+$ at m/z 369/371).

Example 14
3-[4-(*trans*-2-carbamoylethenyl)phenylamino]-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione
3-[4-[*trans*-2-(ethoxycarbonyl)ethenyl]phenylamino)-4-(4-chlorophenyl)-1H-pyrrole-2,5-dione (50mg, 0.126mmol) was dissolved in 2N methanolic ammonia (5ml) and allowed to stand at room temp for 12days. Aqueous ammonia (d 0.88, 5ml) was added and the solution stood at room temp for a further 8days. The mixture was evaporated to dryness and the residue triturated with methanol then ether to give the title compound as a solid.

1H NMR (DMSO-d_6): δ10.75(1H, br), δ9.7 (1H, br), δ7.44 (1H, br), δ7.2 (5H, m), δ7.2 (3H, m), δ6.74 (2H, d), δ6.41 (1H, d).
MS (APCI +ve): $[M+H]^+$ at m/z 368/370 ($C_{19}H_{14}ClN_3O_3$ requires $[M+H]^+$ at m/z 368/370).

Example 15
3-(Indol-1-yl)-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione
Sodium hydride (60% dispersion in mineral oil, 30 mg, 0.75 mmol) was added to a solution of indole (88 mg, 0.75 mmol) in THF (2 mL) at room temperature. The mixture was stirred for 30 minutes prior to the addition of a solution of 1-(*tert*-butyldimethylsilyl)-3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (Intermediate Method 1, 180 mg, 0.5 mmol) in THF (1 mL). The mixture was stirred for 45 minutes then diluted with ethyl acetate (80 mL), washed with dilute hydrochloric

acid (20 mL), dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel using a gradient of hexane-ethyl acetate to afford the title compound, a solid.

^1H NMR (CD_3OD); δ6.42 (1H, d), 6.77 (1H, d), 6.82 (1H, t), 7.00-7.60 (5H, m) and 8.05-8.25 (2H, m).
MS (APCI +ve): $[M+H]^+$ at m/z 334 ($C_{18}H_{11}N_3O_4$ requires $[M+H]^+$ at 334).

Example 16
3-Amino-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione
3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (1.0 g, 4 mmol) was suspended in a mixture of ethanol (20 mL) and aqueous 880 ammonia (5 mL) and the mixture heated to 80°C whilst ammonia gas was bubbled through the mixture for 4 hours. The mixture was cooled and concentrated and the residue chromatographed on silica gel using hexane-ethyl acetate (gradient from 1:1 v/v) as eluent to afford the title compound as a solid.

^1H NMR (CD_3COCD_3); δ6.77 (2H, br), δ7.60 (1H, t), δ8.04 (2H, m), δ8.50 (1H, t) and δ9.33 (1H, br).
MS (APCI +ve): $[M+H]^+$ at m/z 234 ($C_{10}H_7N_3O_4$ requires $[M+H]^+$ at 234).

Intermediate Method 1
1-(*tert*-Butyldimethylsilyl)-3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione
Triethylamine (1.1 mL, 8 mmol) was added to a stirred suspension of *tert*-butylchlorodimethylsilane (0.66 g, 4.4 mmol) and 3-chloro-4-(3-nitrophenyl)-1H-pyrrole-2,5-dione (1.0 g, 4 mmol) in dichloromethane (15 mL) at room temperature. The mixture was stirred overnight then chromatographed directly on silica gel using a hexane-acetone gradient to afford the title compound.

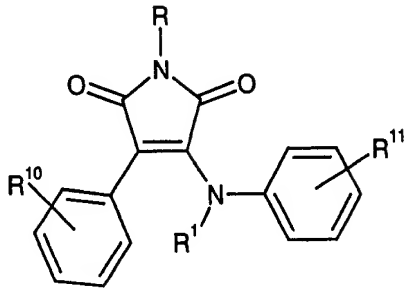
^1H NMR ($CDCl_3$); δ0.51 (6H, s), 0.98 (9H, s), 7.70 (1H, t), 8.27 (2H, m) and 8.80 (1H, m).
MS (APCI +ve): $[M+H]^+$ at m/z 366/368 ($C_{16}H_{19}ClN_2O_4Si$ requires $[M+H]^+$ at 366/368).

The further examples described herein were prepared according to the methods disclosed herein, with particular reference to Examples 1 to 16 above. Examples 1 to 16 themselves are shown as examples A1, A2, A3, A424, B3, A599, F1, F2, F6, A702, A770, A772, A832, A833, D19 and B25 respectively in Tables A, B, D and F.

The following tables of examples illustrate the invention, but do not limit it in any way.

Table A

Encompassing compounds of general formula (XXX-1), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{10} and R^{11} are listed in Table A.



(XXX-1)

Example No.	R	R^1	R^{10}	R^{11}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
A1	H	H	4-Cl	3-Br	377/379/381	1
A2	H	H	4-Cl	4-COPh	402/404 [M]-	2
A3	H	H	3-NO2	3-Br-4-Me	400/402 [M-H]-	3
A4	H	H	H	H	265	1
A5	Me	H	H	H	279	1
A6	H	H	H	4-OMe	295	1
A7	H	H	H	4-Me	279	1
A8	H	H	H	4-Cl	299/301	1

A9	H	H	H	2-Me	277 [M-H]-	1
A10	H	H	H	2-OMe	295	1
A11	H	H	H	4-OnBu	337	1
A12	H	H	H	4-nBu	321	1
A13	Me	H	H	4-Cl	313/315	1
A14	Me	H	H	4-OMe	309	1
A15	Et	H	H	H	293	1
A16	Et	H	H	4-Cl	327/329	1
A17	Et	H	H	4-OMe	323	1
A18	Ph	H	H	H	341	1
A19	Ph	H	H	4-Cl	375/377	1
A20	Ph	H	H	4-OMe	371	1
A21	CH2Ph	H	H	H	355	1
A22	CH2Ph	H	H	4-Cl	389	1
A23	CH2Ph	H	H	4-OMe	385	1
A24	H	H	H	4-SMe	311	1
A25	H	H	H	4-(1-Morpholinyl)	350	1
A26	H	H	H	3-SMe	311	1
A27	H	H	H	3-OPh	357	1
A28	H	H	H	4-F	283	1
A29	H	H	4-Cl	4-OMe	329/331	1
A30	H	H	4-OMe	2-OMe	325	1
A31	H	H	4-OMe	4-OnBu	367	1
A32	H	H	4-OMe	3-OPh	387	1
A33	H	H	4-OMe	3-SMe	341	1
A34	H	H	4-OMe	4-F	313	1
A35	H	H	4-OMe	4-SMe	341	1
A36	H	H	4-OMe	4-nBu	351	1
A37	H	H	4-OMe	H	295	1

A38	H	H	4-OMe	4-Cl	329/331	1
A39	H	H	4-Cl	3-Cl	333/335/337	1
A40	H	H	4-Cl	2-OMe	329/331	1
A41	H	H	4-Cl	4-OnBu	371/373	1
A42	H	H	4-Cl	3-OPh	391/393	1
A43	H	H	4-Cl	3-SMe	345/347	1
A44	H	H	4-Cl	4-CF3	367/369	1
A45	H	H	4-Cl	4-F	317/319	1
A46	H	H	4-Cl	4-SMe	345/347	1
A47	H	H	4-Cl	3-CF3	367/369	1
A48	H	H	4-Cl	4-nBu	355/357	1
A49	H	H	4-Cl	H	299/301	1
A50	H	H	4-Cl	2-Me-4-Cl	347/349/351	1
A51	H	H	4-Cl	4-Cl	333/335/337	1
A52	H	H	4-Cl	2-Me	313/315	1
A53	H	H	4-Cl	2,3-[(-CH=CH-)2]	349/351	1
A54	H	H	2,3-[(-CH=CH-)2]	4-OnBu	387	1
A55	H	H	2,3-[(-CH=CH-)2]	4-F	331 [M-H]-	1
A56	H	H	2,3-[(-CH=CH-)2]	4-SMe	361	1
A57	H	H	2,3-[(-CH=CH-)2]	4-nBu	371	1
A58	H	H	2,3-[(-CH=CH-)2]	H	315	1
A59	H	H	4-OMe	4-OMe	325	1
A60	H	H	4-OMe	3-Cl	329/331	1
A61	H	H	4-OMe	2-Me	309	1
A62	H	H	3,4,5-tri-OMe	4-OMe	385	1
A63	H	H	3,4,5-tri-OMe	H	355	1
A64	H	H	H	3-Cl	299	1
A65	H	H	4-CF3	2-Me	345 [M-H]-	1
A66	H	H	4-CF3	2-Et	359 [M-H]-	1

A67	H	H	4-CF3	2-iPr	375	1
A68	H	H	4-CF3	2-F	349 [M-H]-	1
A69	H	H	4-CF3	2-Cl	365/367 [M-H]-	1
A70	H	H	4-CF3	2-SMe	379	1
A71	H	H	4-CF3	3-SMe	379	1
A72	H	H	4-CF3	3-Me	345 [M-H]-	1
A73	H	H	4-CF3	3-Et	361	1
A74	H	H	4-CF3	3-OMe	363	1
A75	H	H	4-CF3	3-Cl	365/367	1
A76	H	H	4-CF3	3-F	349 [M-H]-	1
A77	H	H	4-CF3	3-Br	409/411 [M-H]-	1
A78	H	H	4-CF3	3-I	457 [M-H]-	1
A79	H	H	4-CF3	3-OCH2Ph	439	1
A80	H	H	4-CF3	3-CONH2	375 [M]-	1
A81	H	H	3,4,5-tri-OMe	4-Cl	389/391	1
A82	H	H	4-Cl	2-Et	327/329	1
A83	H	H	4-Cl	2-iPr	341/343	1
A84	H	H	4-Cl	2-F	317/319	1
A85	H	H	4-Cl	2-SMe	345/347	1
A86	H	H	4-Cl	3-Me	313/315	1
A87	H	H	4-Cl	3-Et	327/329	1
A88	H	H	4-Cl	3-OMe	329/331	1
A89	H	H	4-Cl	3-F	315/317 [M-H]-	1
A90	H	H	4-Cl	3-I	423/425 [M-H]-	1
A91	H	H	4-Cl	3-OCH2Ph	405/407	1
A92	H	H	4-Cl	3-CONH2	342/344	1
A93	H	H	2-CF3	3-SMe	377 [M-H]-	1
A94	H	H	2-CF3	3-Me	347	1
A95	H	H	2-CF3	3-Et	361	1

A96	H	H	4-OMe	4-Me	309	1
A97	H	H	4-OMe	4-tBu	351	1
A98	H	H	4-OMe	3,4-[(CH2)3]	335	1
A99	H	H	4-OMe	3,5-di-Me	323	1
A100	H	H	4-OMe	3-OCH2Ph	401	1
A101	H	H	4-OMe	3-OMe	325	1
A102	H	H	4-OMe	3-I	421	1
A103	H	H	4-OMe	3,4-[OCH2O]	339	1
A104	H	H	4-OMe	3,5-di-OMe	355	1
A105	H	H	3-OMe	4-nBu	351	1
A106	H	H	3-OMe	3-OPh	387	1
A107	H	H	3-OMe	4-SMe	341	1
A108	H	H	3-OMe	4-Me	309	1
A109	H	H	3-OMe	4-tBu	351	1
A110	H	H	3-OMe	3,5-di-Me	323	1
A111	H	H	3-OMe	3-OCH2Ph	401	1
A112	H	H	3-OMe	3-OMe	325	1
A113	H	H	3-OMe	3-I	421	1
A114	H	H	3-OMe	3,4-[OCH2O]	339	1
A115	H	H	3-OMe	3,5-di-OMe	355	1
A116	H	H	3-OMe	4-OMe	325	1
A117	H	H	3-OMe	3,4-[(CH2)3]	335	1
A118	H	H	3-OMe	4-SCF3	395	1
A119	H	H	2-OMe	4-nBu	351	1
A120	H	H	2-OMe	3-OPh	387	1
A121	H	H	2-OMe	4-SMe	341	1
A122	H	H	2-OMe	4-Me	309	1
A123	H	H	2-OMe	4-tBu	351	1
A124	H	H	2-OMe	3,4-[(CH2)3]	335	1

A125	H	H	2-OMe	3,5-di-Me	323	1
A126	H	H	2-OMe	3-OCH2Ph	401	1
A127	H	H	2-OMe	3-OMe	325	1
A128	H	H	2-OMe	3-I	421	1
A129	H	H	2-OMe	3,5-di-OMe	355	1
A130	H	H	2-OMe	4-OMe	325	1
A131	H	H	2-OMe	3-CF3	363	1
A132	H	H	4-OMe	3-CF3	363	1
A133	H	H	3-OMe	3-CF3	363	1
A134	H	H	2-OMe	3,4-[OCH2O]	339	1
A135	H	Me	4-CF3	H	347	1
A136	H	H	4-CF3	H	333	2
A137	H	H	4-CF3	2,3-[(-CH=CH-)2]	383	2
A138	H	H	4-CF3	4-CF3	401	2
A139	H	H	4-CF3	4-CN	358	2
A140	H	H	4-CF3	4-COPh	437	2
A141	H	H	2-CF3	H	333	2
A142	H	H	2-CF3	2-Me	347	2
A143	H	H	4-CF3	2-Me-4-Cl	381/383	2
A144	H	H	4-OMe	3-CH2OH	325	1
A145	H	H	H	2,3-[(-CH=CH-)2]	315	1
A146	H	H	4-Cl	3-OH	315/317	1
A147	H	Me	H	H	279	1
A148	H	Me	4-Ph	H	355	1
A149	H	Me	4-Cl	H	313/315	1
A150	H	Me	4-OMe	H	309	1
A151	H	Me	3-NO2	H	324	1
A152	H	Me	3-OMe	H	309	1
A153	H	H	4-CF3	4-CO2H	377	2

A154	H	H	4-Ph	4-Me	355	1
A155	H	H	4-Ph	4-OnBu	412 [M]-	1
A156	H	H	4-Ph	4-nBu	397	1
A157	H	H	4-Ph	4-SMe	387	1
A158	H	H	4-Ph	2-Me	355	1
A159	H	H	4-Ph	3-SMe	387	1
A160	H	H	4-Ph	3-OPh	433	1
A161	H	H	4-Ph	3-Cl	375/377	1
A162	H	H	4-Ph	2-COMe	383	1
A163	H	H	4-Ph	3-Br	417/419 [M-H]-	1
A164	H	H	4-Ph	3-(5-Oxazolyl)	407 [M]-	1
A165	H	H	4-Ph	3-OH	357	1
A166	H	H	3-NO2	4-Me	324	1
A167	H	H	3-NO2	4-OnBu	382	1
A168	H	H	3-NO2	4-SMe	356	1
A169	H	H	3-NO2	2-Me	324	1
A170	H	H	3-NO2	3-SMe	356	1
A171	H	H	3-NO2	3-OPh	402	1
A172	H	H	3-NO2	3-Cl	344/346	1
A173	H	H	3-NO2	3,5-di-Cl	376/378/380 [M-H]-	1
A174	H	H	3-NO2	3-COMe	350 [M-H]-	1
A175	H	H	3-NO2	3-Br	388/390	1
A176	H	H	3-NO2	3-(5-Oxazolyl)	375 [M-H]-	1
A177	H	H	3-NO2	3-OH	326	1
A178	H	H	3-NO2	4-nBu	366	1
A179	H	H	4-CF3	4-NO2	378	2
A180	H	H	3,4,5-tri-OMe	4-Me	369	1
A181	H	H	3,4,5-tri-OMe	4-OnBu	427	1
A182	H	H	3,4,5-tri-OMe	4-nBu	411	1

A183	H	H	3,4,5-tri-OMe	4-SMe	401	1
A184	H	H	3,4,5-tri-OMe	3-SMe	401	1
A185	H	H	3,4,5-tri-OMe	3-COMe	397	1
A186	H	H	3,4,5-tri-OMe	3-(5-Oxazolyl)	422	1
A187	H	H	3,4,5-tri-OMe	3-OH	371	1
A188	H	H	H	4-CF3	333	1
A189	H	H	4-OMe	4-(CH2)2OH	337 [M-H]-	1
A190	H	H	H	4-(CH2)2OH	309	1
A191	H	H	2-Cl	4-OMe	329	1
A192	H	H	H	3-CF3	331 [M-H]-	1
A193	H	H	4-Cl	4-CN	323/325 [M]-	2
A194	H	H	4-CF3	2,4,6-tri-Me	375	2
A195	H	H	4-Cl	2,3-[(CH2)4]	353/355	1
A196	H	H	4-Cl	4-tBu	355/357	1
A197	H	H	4-Cl	4-CH2P(O)(OEt)2	449/451	1
A198	H	H	4-Cl	4-OPh	391/393	1
A199	H	H	4-Cl	4-(Cyclohexyl)	381/383	1
A200	H	H	4-Cl	2-CH2Ph	389/391	1
A201	H	H	4-Cl	4-Br-3-Cl	411/413/415/417	1
A202	H	H	4-Cl	4-I-3-Cl	459/461/463	1
A203	H	H	4-Cl	3,4-di-Cl	367/369/371/373	1
A204	H	H	4-Cl	3,5-di-Cl	367/369/371/373	1
A205	H	H	4-Cl	3,5-di-Cl-4-OH	383/385/387/389	1
A206	H	H	4-Cl	3,5-di-F	335/337	1
A207	H	H	4-Cl	4-Br	377/379/381	1
A208	H	H	4-Cl	4-I	425/427	1
A209	H	H	4-Cl	3-NO2	344/346	1
A210	H	H	4-Cl	2-OH	315/317	1
A211	H	H	4-Cl	4-OH	315/317	1

A212	H	H	4-Cl	3,5-di-Br-4-Me	469/471/473/475	1
A213	H	H	4-Cl	3,4-[OCH2O]	343/345	1
A214	H	H	4-Cl	3,4-[CH=N-NH]	339/341	1
A215	H	H	4-Cl	3,4-[NH-N=CH]	339/341	1
A216	H	H	4-Cl	3-Br-2-Me	391/393/395	1
A217	H	H	4-Cl	3-Br-4-Me	391/393/395	1
A218	H	H	4-Cl	3-Cl-2-Me	347/349/351	1
A219	H	H	4-Cl	3-F-4-Me	331/333	1
A220	H	H	4-Cl	3-F-6-Me	331/333	1
A221	H	H	4-Cl	4-Me	313/315	1
A222	H	H	4-Cl	2-CH2OH	329/331	1
A223	H	H	4-Cl	3-CH2OH	329/331	1
A224	H	H	4-Cl	4-OH-2-Me	329/331	1
A225	H	H	4-Cl	4-NHCOMe	356/358	1
A226	H	H	4-Cl	2,3-di-Me	327/329	1
A227	H	H	4-Cl	2,4-di-Me	327/329	1
A228	H	H	4-Cl	3,4-di-Me	327/329	1
A229	H	H	4-Cl	3,5-di-Me	327/329	1
A230	H	H	4-Cl	3-CH2OH-6-Me	343/345	1
A231	H	H	4-Cl	4-OMe-2-Me	343/345	1
A232	H	H	4-Cl	4-(CH2)2OH	343/345	1
A233	H	H	4-Cl	3,5-di-OMe	359/361	1
A234	H	H	4-Cl	4-CH2CN	338/340	1
A235	H	H	4-Cl	3,4-[CH=CH-NH]	338/340	1
A236	H	H	4-Cl	3-COMe	341/343	1
A237	H	H	4-Cl	4-CH2CO2H	357/359	1
A238	H	H	4-Cl	3,4-[(CH2)3]	337/339 [M-H]-	1
A239	H	H	4-Cl	4-N(Me)COMe	370/372	1
A240	H	H	4-Cl	3-OiPr	357/359	1

A241	H	H	4-Cl	4-(CH2)2CONH2	370/372	1
A242	H	H	3,4-[OCH2O]	3-OPh	401	1
A243	H	H	4-Cl	4-CONH2	340/342 [M-H]-	3
A244	H	H	4-F	2-Me	297	1
A245	H	H	4-F	3-SMe	329	1
A246	H	H	4-F	3-Cl	317/319	1
A247	H	H	4-F	4-Cl-2-Me	331/333	1
A248	H	H	4-F	3-OPh	375	1
A249	H	H	4-F	4-SMe	329	1
A250	H	H	4-F	4-tBu	339	1
A251	H	H	4-F	3,4-[(CH2)3]	323	1
A252	H	H	2-OMe	3-Me	309	1
A253	H	H	2-OMe	3-F	313	1
A254	H	H	2-OMe	2-F	313	1
A255	H	H	2-OMe	4-Cl-2-Me	343/345	1
A256	H	H	2-OMe	2-Me	309	1
A257	H	H	2-OMe	3-SMe	341	1
A258	H	H	3-Cl	2-Me	313/315	1
A259	H	H	3-Cl	3-SMe	345/347	1
A260	H	H	3-Cl	3-Cl	333/335/337	1
A261	H	H	3-Cl	4-Cl-2-Me	347/349/351	1
A262	H	H	3-Cl	3-OPh	391/393	1
A263	H	H	3-Cl	4-SMe	345/347	1
A264	H	H	3-Cl	4-tBu	355/357	1
A265	H	H	3-Cl	3,4-[(CH2)3]	339/341	1
A266	H	H	3,4-[(-CH=CH-)2]	3-Me	329	1
A267	H	H	3,4-[(-CH=CH-)2]	3-F	333	1
A268	H	H	3,4-[(-CH=CH-)2]	4-Cl-2-Me	363/365	1
A269	H	H	3,4-[(-CH=CH-)2]	2-Me	329	1

A270	H	H	3,4-[(-CH=CH-)2]	3-SMe	361	1
A271	H	H	3,4-[(-CH=CH-)2]	3-Cl	349/351	1
A272	H	H	4-I	2-Me	405	1
A273	H	H	4-I	3-SMe	437	1
A274	H	H	4-I	3-Cl	425/427	1
A275	H	H	4-I	4-Cl-2-Me	439/441	1
A276	H	H	4-I	3-OPh	483	1
A277	H	H	4-I	4-SMe	437	1
A278	H	H	4-I	4-tBu	447	1
A279	H	H	4-I	3,4-[(CH2)3]	431	1
A280	H	H	4-OMe	3-Me	309	1
A281	H	H	4-OMe	3-F	313	1
A282	H	H	3-OMe	2-Me	309	1
A283	H	H	3-OMe	3-SMe	341	1
A284	H	H	3-OMe	3-Cl	329/331	1
A285	H	H	2-OMe	3-Cl	329/331	1
A286	H	H	4-F	3-Br	361/363	1
A287	H	H	4-OMe	3-Br	373/375	1
A288	H	H	3,4-[(-CH=CH-)2]	3-Br	393/395	1
A289	H	H	4-I	3-Br	469/471	1
A290	H	H	4-Cl	4-NO2	342/344 [M-H]-	3
A291	H	H	3,4-di-Cl	3-Br	411/413/415/417	1
A292	H	H	3-Cl	3-Br	377/379/381	1
A293	H	H	2-Cl	3-OPh	391/393	3
A294	H	H	2-Cl	3-Cl	333/335	3
A295	H	H	2-Cl	3-SMe	345/347	1
A296	H	H	2-Cl	4-SMe	345/347	1
A297	H	H	3-OMe	4-CONH2	337 [M]-	3
A298	H	H	4-Cl	4-CO2H	297/299 Fragment ion	3

A299	H	H	4-OMe	4-CN	[M-CO2H]-	
A300	H	H	2-Cl	4-nBu	320	3
A301	H	H	2-Cl	3-Br	355/357	1
A302	H	H	2-Cl	4-Me	375/377/379 [M]-	1
A303	H	H	4-Cl	3-Cl-6-Me	313/315	1
A304	H	H	3-NO2	3-Cl-4-Me	347/349/351	3
A305	H	H	3-NO2	4-COPh	356/358 [M-H]-	3
A306	H	H	3,5-di-F	3-Br	414	3
A307	H	H	3-CF3	3-Br	379/381	1
A308	H	H	4-Me	3-Br	411/413	1
A309	H	H	4-Br	3-SMe	357/359	1
A310	H	H	4-Br	4-Me	389/391	1
A311	H	H	4-Br	3,5-di-Cl	357/359	1
A312	H	H	4-Br	3-OPh	409/411/413/415 [M-H]-	1
A313	H	H	4-Br	3,4-[(CH2)3]	435/437	1
A314	H	H	4-Me	3-SMe	383/385	1
A315	H	H	4-Me	4-Me	325	1
A316	H	H	4-Me	3-OPh	293	1
A317	H	H	4-Me	3,4-[(CH2)3]	371	1
A318	H	H	4-Me	4-SMe	319	1
A319	H	H	4-SMe	3-SMe	325	1
A320	H	H	4-SMe	4-Me	357	1
A321	H	H	4-SMe	3-OPh	325	1
A322	H	H	4-SMe	3,4-[(CH2)3]	403	1
A323	H	H	4-SMe	4-SMe	351	1
A324	H	H	3-CF3	3-SMe	357	1
A325	H	H	3-CF3	4-Me	379	1
A326	H	H	3-CF3	3,5-di-Cl	347	1
					399/401/403 [M-H]-	1

A327	H	H	3-CF3	3-OPh	425	1
A328	H	H	3-CF3	3,4-[(CH2)3]	373	1
A329	H	H	3-CF3	4-SMe	379	1
A330	H	H	3,5-di-F	3-SMe	347	1
A331	H	H	3,5-di-F	4-Me	315	1
A332	H	H	3,5-di-F	3,5-di-Cl	367/369/371 [M]-	1
A333	H	H	3,5-di-F	3-OPh	393	1
A334	H	H	3,5-di-F	3,4-[(CH2)3]	341	1
A335	H	H	3,5-di-F	4-SMe	347	1
A336	H	H	3,4-di-Cl	3-SMe	379/381/383	1
A337	H	H	3,4-di-Cl	4-Me	347/349/351	1
A338	H	H	3,4-di-Cl	3,5-di-Cl	399/401/403/405/407 [M-H]-	1
A339	H	H	3,4-di-Cl	3-OPh	423/425/427 [M]-	1
A340	H	H	3,4-di-Cl	3,4-[(CH2)3]	373/375/377	1
A341	H	H	3,4-di-Cl	4-SMe	379/381/383	1
A342	H	H	3-Br	3-SMe	389/391	1
A343	H	H	3-Br	4-Me	355/357 [M]-	1
A344	H	H	3-Br	3,5-di-Cl	409/411/413/415 [M-H]-	1
A345	H	H	3-Br	3-OPh	435/437	1
A346	H	H	3-Br	3,4-[(CH2)3]	383/385	1
A347	H	H	3-Br	4-SMe	389/391	1
A348	H	H	4-NO2	3-SMe	356	1
A349	H	H	4-NO2	4-Me	324	1
A350	H	H	4-NO2	3,5-di-Cl	376/378/380 [M-H]-	1
A351	H	H	4-NO2	3-OPh	402	1
A352	H	H	4-NO2	3,4-[(CH2)3]	350	1
A353	H	H	4-NO2	4-SMe	356	1
A354	H	H	4-Br	4-SMe	389/391	1

A355	H	H	3-NO2	4-NO2	353 [M]-	3
A356	H	H	3-NO2	3,5-di-Cl-4-OH	392/394/396 [M-H]-	1
A357	H	H	3-NO2	4-tBu	366	1
A358	H	H	3-NO2	3,5-di-Br-4-OH	482/484/486	1
A359	H	H	3-NO2	3,4-[(CH2)3]	350	1
A360	H	H	3-NO2	3-Br-4-OCF3	470/472[M-H]-	1
A361	H	H	3-NO2	3-Br-5-CF3	454/456[M-H]-	1
A362	H	H	3-NO2	4-CH2CN	349	1
A363	H	H	3-NO2	4-(CH2)2CONH2	381	1
A364	H	H	3-NO2	3-F	326[M-H]-	1
A365	H	H	3-NO2	3-F-4-Me	342	1
A366	H	H	3-NO2	4-Cl	342/344[M-H]-	1
A367	H	H	3-NO2	4-OMe	340	1
A368	H	H	3-NO2	3-Et	338	1
A369	H	H	3-NO2	2-F	328	1
A370	H	H	3-NO2	3,5-di-F	344[M-H]-	1
A371	H	H	3-NO2	3,4-[S-CH=N]	367	1
A372	H	H	3-NO2	4-OPh	402	1
A373	H	H	3-NO2	4-trans-CH=CHCO2H	378[M-H]-	1
A374	H	H	3-NO2	4-OCH2Ph	416	1
A375	H	H	3-NO2	3-CO(CH2)2CO2Me	422[M-H]-	1
A376	H	H	3-NO2	3-NO2	353 [M]-	3
A377	H	H	3-NO2	4-CN	333 [M]-	3
A378	H	H	4-Cl	4-OH-3-CO2H	359/361	1
A379	H	H	4-Cl	3-CO2H	341/343 [M-H]-	1
A380	H	H	4-Cl	4-SCH2CO2Me	403/405	1
A381	H	H	4-Cl	4-OH-3-NO2	360/362	1
A382	H	H	4-Cl	4-(CH2)2CO2H	371/373	1
A383	H	H	4-Cl	4-Cl-3-CO2H	375/377/379 [M-H]-	1

A384	H	H	4-Cl	4-(CH2)3CO2H	385/387	1
A385	H	H	4-Cl	3-SO2CF3	429/431[M-H]-	1
A386	H	H	4-Cl	3-COPh	403/405	1
A387	H	H	4-Cl	3,5-di-Br-4-OH	471/473/475/477	1
A388	H	H	4-Cl	4-CPh3	541/543	1
A389	H	H	4-Cl	3-CH2CO2H	355/357 [M-H]-	1
A390	H	H	4-Cl	4-(1-Adamantyl)	433/435	1
A391	H	H	4-Cl	3-CO2H-4-[S-(2-CO2H-Ph)]	373/375 Fragment ion [M-C7H5O2]-	1
A392	H	H	4-Cl	2-[O(CH2)2OMe]-5-(CH2)2CO2H	443/445 [M-H]-	1
A393	H	H	4-Cl	3-Br-4-Cl	411/413/415/417	1
A394	H	H	4-Cl	2-OPh	391/393	1
A395	H	H	4-Cl	4-CH2SO2NHMe	311/313 Fragment ion [M – CH4NO2S]+	1
A396	H	H	3-NO2	4-CO2H	352 [M-H]-	3
A397	H	H	3-NO2	3-COPh	414	3
A398	H	H	4-Cl	3-CH2CO2Me	371/373	1
A399	H	H	4-OH	3-Br	359/361	4
A400	H	H	4-Br	4-COPh	447/449	3
A401	H	H	4-SMe	4-COPh	415	3
A402	H	H	4-OH	4-SMe	327	4
A403	H	H	4-iPr	3-SMe	351[M-H]-	1
A404	H	H	4-iPr	4-Me	319[M-H]-	1
A405	H	H	4-iPr	3,4-[(CH2)3]	345[M-H]-	1
A406	H	H	3,5-di-Me	3-SMe	337[M-H]-	1
A407	H	H	3,5-di-Me	4-Me	305[M-H]-	1
A408	H	H	3,5-di-Me	3,4-[(CH2)3]	331[M-H]-	1
A409	H	H	3,5-di-Me	4-SMe	337[M-H]-	1

A410	H	H	4-iPr	4-SMe	351[M-H]-	1
A411	H	H	2-Br	3-SMe	387/389[M-H]-	1
A412	H	H	2-Br	4-Me	355/357[M-H]-	1
A413	H	H	2-Br	3,4-[(CH2)3]	381/383[M-H]-	1
A414	H	H	2-Br	4-SMe	387/389[M-H]-	1
A415	H	H	3,5-bis-CF3	3-SMe	446[M]-	1
A416	H	H	3,5-bis-CF3	4-Me	414[M]-	1
A417	H	H	3,5-bis-CF3	3,5-di-Cl	468/470/472 [M]-	1
A418	H	H	3,5-bis-CF3	3,4-[(CH2)3]	440[M]-	1
A419	H	H	3,5-bis-CF3	4-SMe	446[M]-	1
A420	H	H	4-OPh	3-SMe	401[M-H]-	1
A421	H	H	4-OPh	4-Me	369[M]-	1
A422	H	H	4-OPh	3,4-[(CH2)3]	395[M-H]-	1
A423	H	H	4-OPh	4-SMe	401[M-H]-	1
A424	H	H	4-OH	4-Me	295	4
A425	H	H	4-OCH2Ph	3-SMe	415[M-H]-	1
A426	H	H	4-OCH2Ph	3,4-[(CH2)3]	409[M-H]-	1
A427	H	H	4-OCH2Ph	4-SMe	415[M-H]-	1
A428	H	H	3,4-di-OMe	3-SMe	371	1
A429	H	H	3,4-di-OMe	4-Me	337[M-H]-	1
A430	H	H	3,4-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A431	H	H	3-Cl-4-OMe	4-SMe	373/375 [M-H]-	1
A432	H	H	3-Cl-4-OMe	3-SMe	373/375 [M-H]-	1
A433	H	H	3-Cl-4-OMe	4-Me	341/343 [M-H]-	1
A434	H	H	3-Cl-4-OMe	3,4-[(CH2)3]	369/371	1
A435	H	H	3-NO2	4-COMe	352	3
A436	H	H	4-OH	3-OPh	371[M-H]-	4
A437	H	H	4-OH	3-Br-4-Me	371/373[M-H]-	4
A438	H	H	4-OH	3,4-[(CH2)3]	321	4

A439	H	H	3,5-di-Me	3-OPh	383[M-H]-	1
A440	H	H	2-Br	3-OPh	434[M-H]-	1
A441	H	H	3,5-bis-CF3	3-OPh	492[M]-	1
A442	H	H	4-OCH2Ph	3-OPh	461[M-H]-	1
A443	H	H	3-Cl-4-OMe	3-OPh	419/421 [M-H]-	1
A444	H	H	3,4-di-OMe	3-OPh	415[M-H]-	1
A445	H	H	4-OPh	3-OPh	447[M-H]-	1
A446	H	H	4-OCH2Ph	4-Me	383[M-H]-	1
A447	H	H	2-Cl	3-Cl-4-Me	347/349/351	3
A448	H	H	3,4-[OCH2O]	3-SMe	353[M-H]-	1
A449	H	H	3,4-[OCH2O]	4-Me	323	1
A450	H	H	3,4-[OCH2O]	3,4-[(CH2)3]	349	1
A451	H	H	3,4-[OCH2O]	4-SMe	355	1
A452	H	H	3,4-[OCH2O]	3-Br	387/389	1
A453	H	H	3,4-[OCH2O]	3-Br-4-Me	401/403	1
A454	H	H	2-Me	4-Me	293	1
A455	H	H	2-Me	3,4-[(CH2)3]	319	1
A456	H	H	2-Me	4-SMe	325	1
A457	H	H	3-Me	3-OPh	371	1
A458	H	H	3-Br	4-Cl	375/377/379 [M-H]-	1
A459	H	H	4-iPr	3-OPh	397[M-H]-	1
A460	H	H	4-CH2OMe	3-SMe	353[M-H]-	1
A461	H	H	4-CH2OMe	4-Me	321[M-H]-	1
A462	H	H	4-CH2OMe	H	307[M-H]-	1
A463	H	H	4-CH2OMe	3-OPh	399[M-H]-	1
A464	H	H	4-CH2OMe	3,4-[(CH2)3]	347[M-H]-	1
A465	H	H	4-CH2OMe	4-SMe	353[M-H]-	1
A466	H	H	4-CH2OMe	3-Br	385/387[M-H]-	1
A467	H	H	4-CH2OMe	3-Br-4-Me	399/401[M-H]-	1

A468	H	H	2-Me	4-Cl	313/315	1
A469	H	H	2,5-di-OMe	3-SMe	369[M-H]-	1
A470	H	H	2,5-di-OMe	4-Me	337[M-H]-	1
A471	H	H	2,5-di-OMe	H	323[M-H]-	1
A472	H	H	2,5-di-OMe	3-OPh	415[M-H]-	1
A473	H	H	2,5-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A474	H	H	2,5-di-OMe	4-SMe	369[M-H]-	1
A475	H	H	2,5-di-OMe	3-Br	401/403 [M-H]-	1
A476	H	H	2,5-di-OMe	3-Br-4-Me	415/417[M-H]-	1
A477	H	H	4-OCF3	3-SMe	393[M-H]-	1
A478	H	H	4-OCF3	4-Me	361[M-H]-	1
A479	H	H	4-OCF3	H	347[M-H]-	1
A480	H	H	4-OCF3	3-OPh	439[M-H]-	1
A481	H	H	4-OCF3	3,4-[(CH2)3]	387[M-H]-	1
A482	H	H	4-OCF3	3-Br	425/427[M-H]-	1
A483	H	H	4-OCF3	3-Br-4-Me	439/441 [M-H]-	1
A484	H	H	4-OCF3	4-SMe	393[M-H]-	1
A485	H	H	3-SCF3	3-SMe	409[M-H]-	1
A486	H	H	3-SCF3	4-Me	377[M-H]-	1
A487	H	H	3-SCF3	H	363[M-H]-	1
A488	H	H	3-SCF3	3-OPh	455[M-H]-	1
A489	H	H	3-SCF3	3,4-[(CH2)3]	403[M-H]-	1
A490	H	H	3-SCF3	4-SMe	409[M-H]-	1
A491	H	H	3-SCF3	3-Br	441/443[M-H]-	1
A492	H	H	3-SCF3	3-Br-4-Me	455/457[M-H]-	1
A493	H	H	3-Cl	4-Cl	333/335/337	1
A494	H	H	4-Cl	3,4-[S-CH=N]	356/358	1
A495	H	H	2-OMe	3,4-[S-CH=N]	352	1
A496	H	H	4-OMe	3,4-[S-CH=N]	352	1

A497	H	H	4-Br	4-CH=CHCO2H	411/413 [M-H]-	1
A498	H	H	4-Br	4-CH(OMe)Me	401/403	1
A499	H	H	2-Me	3-SMe	325	1
A500	H	H	2-Me	3-Br-4-Me	371/373	1
A501	H	H	3-F	3-SMe	329	1
A502	H	H	3-F	4-Me	297	1
A503	H	H	3-F	3,5-di-Cl	351/353/355	1
A504	H	H	3-F	3-OPh	375	1
A505	H	H	3-F	3,4-[(CH2)3]	323	1
A506	H	H	3-F	4-SMe	329	1
A507	H	H	3-F	3-Br	361/363	1
A508	H	H	3-F	3-Br-4-Me	375/377	1
A509	H	H	2,4-di-Cl	3-SMe	379/381/383	1
A510	H	H	2,4-di-Cl	4-Me	347/349/350	1
A511	H	H	2,4-di-Cl	3-OPh	425/427/429	1
A512	H	H	2,4-di-Cl	3,4-[(CH2)3]	373/375/377	1
A513	H	H	2,4-di-Cl	4-SMe	379/381/383	1
A514	H	H	2,4-di-Cl	3-Br	411/413/415/417	1
A515	H	H	2,4-di-Cl	3-Br-4-Me	425/427/429/431	1
A516	H	H	3-Me	3-SMe	325	1
A517	H	H	3-Me	4-Me	293	1
A518	H	H	3-Me	3,4-[(CH2)3]	319	1
A519	H	H	3-Me	4-SMe	325	1
A520	H	H	3-Me	3-Br	357/359	1
A521	H	H	3-Me	3-Br-4-Me	371/373	1
A522	H	H	4-Cl-3-NO2	3-SMe	388/390[M-H]-	1
A523	H	H	4-Cl-3-NO2	4-Me	356/358[M-H]-	1
A524	H	H	4-Cl-3-NO2	3,5-di-Cl	410/412/414/416[M-H]-	1
A525	H	H	4-Cl-3-NO2	3-OPh	434/436[M-H]-	1

A526	H	H	4-Cl-3-NO2	3,4-[(CH2)3]	384/386	1
A527	H	H	4-Cl-3-NO2	4-SMe	390/392	1
A528	H	H	4-Cl-3-NO2	3-Br-4-Me	434/436/438[M-H]-	1
A529	H	H	4-OH	3,4-[S-CH=N]	338	4
A530	H	H	4-SMe	3,4-[S-CH=N]	368	1
A531	H	H	4-I	3,4-[S-CH=N]	448	1
A532	H	H	2-Cl	3,4-[S-CH=N]	356/358	1
A533	H	H	4-Cl-3-NO2	3-Br	420/422/424[M-H]-	1
A534	H	H	3-NO2	3-CH2OH	338[M-H]-	1
A535	H	H	3-NO2	3-CONH2	351[M-H]-	1
A536	H	H	3-NO2	3-OCH2CO2Et	410[M-H]-	1
A537	H	H	3-NO2	3,4-di-Me	336[M-H]-	1
A538	H	H	3-NO2	3-CO2H	352[M-H]-	1
A539	H	H	3-NO2	3,4-[OCH2O]	352[M-H]-	1
A540	H	H	3-NO2	3-CH2CO2Me	380[M-H]-	1
A541	H	H	3-NO2	3-OCH2CO2Me	396[M-H]-	1
A542	H	H	4-Br	3-Cl-4-Me	391/393/395	1
A543	H	H	4-Me	3-Cl-4-Me	327/329	1
A544	H	H	4-SMe	3-Cl-4-Me	359/361	1
A545	H	H	2-OMe	3-Cl-4-Me	343/345	1
A546	H	H	4-OMe	3-Cl-4-Me	343/345	1
A547	H	H	2-Cl	3-Br-4-Me	391/393/395	1
A548	H	H	4-Br	3-Br-4-Me	435/437/439	1
A549	H	H	4-Me	3-Br-4-Me	371/373	1
A550	H	H	4-SMe	3-Br-4-Me	403/405	1
A551	H	H	2-OMe	3-Br-4-Me	387/389	1
A552	H	H	4-OMe	3-Br-4-Me	387/389	1
A553	H	H	2-Cl	H	299/301	1
A554	H	H	4-Br	H	343/345	1

A555	H	H	4-Me	H	279	1
A556	H	H	4-SMe	H	311	1
A557	H	H	2-OMe	H	295	1
A558	H	H	3-NO2	3-Cl-4-OH	358/360 [M-H]-	1
A559	H	H	3-NO2	3-Cl-4-OMe	374/376	1
A560	H	H	3-NO2	3-F-4-OMe	358	1
A561	H	H	3-NO2	3,5-di-Br	464/466/468 [M-H]-	1
A562	H	H	3-NO2	3,5-di-Br-4-Me	478/480/482 [M-H]-	1
A563	H	H	3-NO2	3,5-di-Me	338	1
A564	H	H	3-NO2	H	310	1
A565	H	H	2-Me	3-OPh	371	1
A566	H	H	3-NO2	4-(CH2)2OH	352 [M-H]-	1
A567	H	H	3-NO2	4-CH2CO2H	366 [M-H]-	1
A568	H	H	3-NO2	4-CH2P(O)(OEt)2	460	1
A569	H	H	3-NO2	4-CH2SO2NHMe	415 [M-H]-	1
A570	H	H	3-NO2	4-SCH2CO2H	398 [M-H]-	1
A571	H	H	3-NO2	4-OH	324 [M-H]-	1
A572	H	H	3-NO2	4-(CH2)3CO2H	394 [M-H]-	1
A573	H	H	3-NO2	4-CH2CO2Me	380 [M-H]-	1
A574	H	H	3-NO2	4-SCH2CO2Me	412 [M-H]-	1
A575	H	H	3-NO2	4-(CH2)3CO2Me	410	1
A576	H	H	3-NO2	3,4-[CH=N-NH]	350	1
A577	H	H	3-NO2	3,4-[NH-N=CH]	350	1
A578	H	H	4-Me	3,4-[S-CH=N]	336	1
A579	H	H	4-Br	3,4-[S-CH=N]	400/402	1
A580	H	H	3,5-di-F	3,4-[S-CH=N]	358	1
A581	H	H	3-NO2	2-Ph	384 [M-H]-	1
A582	H	H	2-OMe	3-Et	323	1
A583	H	H	2-OMe	3-OH	311	1

A584	H	H	2-OMe	3-Br	373/375	1
A585	H	H	2-OMe	3-COMe	337	1
A586	H	H	2-OMe	3-COPh	399	1
A587	H	H	2-OMe	3-F-4-Me	327	1
A588	H	H	2-OMe	3,5-di-Br-4-OH	467/469/471	1
A589	H	H	2-OMe	4-CH2CN	334	1
A590	H	H	2-OMe	4-(CH2)2CONH2	366	1
A591	H	H	2-OMe	4-Cl	329/321	1
A592	H	H	2-OMe	4-OPh	387	1
A593	H	H	2-OMe	4-OCH2Ph	401	1
A594	H	H	2-OMe	3-F-4-OMe	343	1
A595	H	H	2-OMe	3-Cl-4-OMe	357/359 [M-H]-	1
A596	H	H	2-OMe	3-Cl-4-OH	345/347	1
A597	H	H	2-OMe	4-Br-3-Cl	407/409/411	1
A598	H	H	2-OMe	3-Br-4-OCF3	457/459	1
A599	H	H	3-NH2	3,4-[(CH2)3]	320	6
A600	H	H	4-SMe	2-Ph	385 [M-H]-	1
A601	H	H	3-NO2	4-I	435 [M]-	1
A602	H	H	2-OMe	3-NO2	340	1
A603	H	H	2-OMe	3,5-di-F	331	1
A604	H	H	2-OMe	3-Br-5-CF3	441/443	1
A605	H	H	2-OMe	3,5-di-Cl-4-OH	379/381/383	1
A606	H	H	2-OMe	4-trans-CH=CHCO2H	363 [M-H]-	1
A607	H	H	3-OPh	4-Me	371	1
A608	H	H	3-OPh	3-Br	433/435 [M-H]-	1
A609	H	H	3-OPh	4-SMe	401 [M-H]-	1
A610	H	H	3-OPh	3-OPh	447 [M-H]-	1
A611	H	H	3-OPh	3,4-[(CH2)3]	395 [M-H]-	1
A612	H	H	3-OPh	H	357	1

A613	H	H	3-OPh	3-SMe	403	1
A614	H	H	3-OPh	3-Br-4-Me	447/449 [M-H]-	1
A615	H	H	4-OnBu	4-Me	349 [M-H]-	1
A616	H	H	4-OnBu	3-OPh	428 [M]-	1
A617	H	H	4-OnBu	3,4-[(CH2)3]	377	1
A618	H	H	4-OnBu	H	337	1
A619	H	H	4-OnBu	3-SMe	383	1
A620	H	H	4-OnBu	3-Br-4-Me	427/429 [M-H]-	1
A621	H	H	2,6-di-Cl	4-Me	347/349/351	1
A622	H	H	2,6-di-Cl	H	331/333/335 [M-H]-	1
A623	H	H	2,6-di-Cl	3-SMe	377/379/381 [M-H]-	1
A624	H	H	4-SMe	3-Br	389/391	1
A625	H	H	4-SMe	3-Cl	345/347	1
A626	H	H	3,5-di-F	3-NO2	344 [M-H]-	1
A627	H	H	2-Cl	3,4-di-Me	327/329	1
A628	H	H	4-Br	3,4-di-Me	369/371 [M-H]-	1
A629	H	H	4-Br	3-Br	419/421/423 [M-H]-	1
A630	H	H	4-Br	3-Cl	375/377/379 [M-H]-	1
A631	H	H	3-Br	3-NO2	386/388 [M-H]-	1
A632	H	H	2-OMe	3,4-di-Me	323	1
A633	H	H	3-OMe	3,4-di-Me	323	1
A634	H	H	3-OPh	3,4-di-Me	385	1
A635	H	H	4-SMe	3,4-di-Me	337 [M-H]-	1
A636	H	H	3-OPh	4-Br	433/435 [M-H]-	1
A637	H	H	4-Me	3-Cl	313/315	1
A638	H	H	2-OMe	4-(CH2)2NHCO2tBu	436 [M-H]-	1
A639	H	H	3-NO2	2,3-[(CH2)4]	362 [M-H]-	1
A640	H	H	3-Cl	3-NO2	342/344 [M-H]-	1
A641	H	H	2-OMe	4-CH2NHCO2tBu	422 [M-H]-	1

A642	H	H	4-OnBu	4-SMe	383	1
A643	H	H	4-C(OMe)2Ph	3-Cl	417/419 Fragment ion [M-OMe]+	1
A644	H	H	4-COPh	3-Cl	403/405	1
A645	H	H	3-NO2-4-OMe	3-Cl	374/376	1
A646	H	H	2-NO2	3-Cl	344/346	1
A647	H	H	2,4-di-OMe	3-SMe	369[M-H]-	1
A648	H	H	2,4-di-OMe	4-Me	337[M-H]-	1
A649	H	H	2,4-di-OMe	H	323[M-H]-	1
A650	H	H	2,4-di-OMe	3-OPh	415[M-H]-	1
A651	H	H	2,4-di-OMe	3,4-[(CH2)3]	363[M-H]-	1
A652	H	H	2,4-di-OMe	4-SMe	369[M-H]-	1
A653	H	H	2,4-di-OMe	3-Br	403/404	1
A654	H	H	2,4-di-OMe	3-Br-4-Me	415/417[M-H]-	1
A655	H	H	3-NO2	3-Cl-4-SMe	388/390 [M-H]-	1
A656	H	H	2-OMe	3-Cl-4-SMe	373/375 [M-H]-	1
A657	H	H	3-NO2	4-CH2NHBoc	437 [M-H]-	1
A658	H	H	4-Br	4-NMe2	386/388	1
A659	H	H	2-OMe	4-NMe2	338	1
A660	H	H	3-NO2	4-NMe2	353	1
A661	H	H	3-NO2	3-OMe	373/375	1
A662	H	H	3-NO2	3-OMe	340	1
A663	H	H	4-Br	3,4-di-OMe	403/405	1
A664	H	H	2-OMe	3,4-di-OMe	355	1
A665	H	H	3-NO2	3,4-di-OMe	370	1
A666	H	H	4-SO2Me	3-Br-4-Me	433/435[M-H]-	1
A667	H	H	4-SO2Me	3-Br	419/421[M-H]-	1
A668	H	H	4-SO2Me	4-SMe	388[M]-	1
A669	H	H	4-SO2Me	3,4-[(CH2)3]	382[M]-	1

A670	H	H	4-SO2Me	3-OPh	434[M]-	1
A671	H	H	4-SO2Me	H	342[M]-	1
A672	H	H	4-SO2Me	4-Me	356[M]-	1
A673	H	H	4-SO2Me	3-SMe	388[M]-	1
A674	H	H	2-F	3-SMe	327[M-H]-	1
A675	H	H	2-F	4-Me	295[M-H]-	1
A676	H	H	2-F	3-OPh	373[M-H]-	1
A677	H	H	2-F	3,4-[(CH2)3]	321[M-H]-	1
A678	H	H	2-F	4-SMe	327[M-H]-	1
A679	H	H	2-F	3-Br	359/361[M-H]-	1
A680	H	H	2-F	3-Br-4-Me	373/375[M-H]-	1
A681	H	H	2,3-di-F	3-Br-4-Me	391/393[M-H]-	1
A682	H	H	2,3-di-F	3-Br	377/379[M-H]-	1
A683	H	H	2,3-di-F	4-SMe	345[M-H]-	1
A684	H	H	2,3-di-F	3,4-[(CH2)3]	339[M-H]-	1
A685	H	H	2,3-di-F	3-OPh	391[M-H]-	1
A686	H	H	2,3-di-F	H	299[M-H]-	1
A687	H	H	2,3-di-F	4-Me	313[M-H]-	1
A688	H	H	2,3-di-F	3-SMe	345[M-H]-	1
A689	H	H	3-NO2	3,4-[N=N-NH]	351	1
A690	H	Me	3-NO2	2-Me	338	1
A691	H	H	3-NO2	2-OH	326	1
A692	H	H	3-NO2	3-CF3	376[M-H]-	1
A693	H	H	3-NO2	3-OCH2Ph	414[M-H]-	1
A694	H	H	3-NO2	3-CO2H-4-Cl	386[M-H]-	1
A695	H	H	3-NO2	3-CO2Me	368	1
A696	H	H	3-NO2	2-OMe	340	1
A697	H	H	3-NO2	3-I	436	1
A698	H	H	3-NO2	3-CO2Me-4-Cl	402/404	1

A699	H	H	3-NO2-4-OMe	3,4-[(CH2)3]	380	1
A700	H	H	3-NO2-4-OMe	3-Br-4-Me	432/434	1
A701	H	H	3-NO2	4-(CH2)2NHBoc	451 [M-H]-	1
A702	H	H	2-OMe	4-(CH2)2NH2	338	10
A703	H	H	2-F	H	281[M-H]-	1
A704	H	H	4-Br	4-CH2NHBoc	470/472 [M-H]-	
A705	H	H	4-I	3-F-4-Me	421 [M-H]-	1
A706	H	H	2-OCH2Ph	3-Cl	405/407	1
A707	H	H	2-Cl	3,5-di-Cl-4-OH	383/385/387/389	1
A708	H	H	2-Cl	3,5-di-Br-4-OH	471/473/475/477	1
A709	H	H	2-Cl	3-CO2H-4-Cl	377/379/381	1
A710	H	H	2-Cl	3-CO2H	343/345	1
A711	H	H	2-Cl	3-OH	315/317	1
A712	H	H	2-Cl	3,4-[OCH2O]	343/345	1
A713	H	H	2-Cl	3,4-[(CH2)3]	339/341	1
A714	H	H	H	3,5-di-Cl-4-OH	349/351/353	1
A715	H	H	H	3,5-di-Br-4-OH	437/439/441	1
A716	H	H	H	3-CO2H-4-Cl	343/345	1
A717	H	H	H	3-CO2H	309	1
A718	H	H	H	3-OH	281	1
A719	H	H	H	3,4-[OCH2O]	309	1
A720	H	H	H	3,4-[(CH2)3]	305	1
A721	H	H	3-NO2-4-OMe	H	340	1
A722	H	H	3-NO2-4-OMe	4-SMe	386	1
A723	H	H	4-Br	3,5-di-Cl-4-OH	427/429/431/433	1
A724	H	H	4-Br	3,5-di-Br-4-OH	515/517/519/521	1
A725	H	H	4-Br	3-CO2H-4-Cl	419/421/423 [M-H]-	1
A726	H	H	4-Br	3-CO2H	387/389	1
A727	H	H	4-Br	3-OH	359/361	1

A728	H	H	4-Br	3,4-[OCH2O]	387/389	1
A729	H	H	4-I	3,5-di-Cl-4-OH	475/477/479	1
A730	H	H	4-I	3,5-di-Br-4-OH	563/565/567	1
A731	H	H	4-I	3-CO2H-4-Cl	469/471	1
A732	H	H	4-I	3-CO2H	435	1
A733	H	H	4-I	3-OH	407	1
A734	H	H	4-I	3,4-[OCH2O]	435	1
A735	H	H	3-Me	3,5-di-Cl-4-OH	363/365/367	1
A736	H	H	3-Me	3,5-di-Br-4-OH	451/453/455	1
A737	H	H	3-Me	3-CO2H-4-Cl	357/359	1
A738	H	H	3-Me	3-CO2H	323	1
A739	H	H	3-Me	3-OH	295	1
A740	H	H	3-Me	3,4-[OCH2O]	323	1
A741	H	H	3-F	3,5-di-Cl-4-OH	367/369/371	1
A742	H	H	3-F	3,5-di-Br-4-OH	455/457/459	1
A743	H	H	3-F	3-CO2H-4-Cl	361/363	1
A744	H	H	3-F	3-CO2H	327	1
A745	H	H	3-F	3-OH	299	1
A746	H	H	3-F	3,4-[OCH2O]	327	1
A747	H	H	4-OMe	3,5-di-Cl-4-OH	379/381/383	1
A748	H	H	4-OMe	3,5-di-Br-4-OH	467/469/471	1
A749	H	H	4-OMe	3-CO2H	339	1
A750	H	H	4-OMe	3-OH	311	1
A751	H	H	3-OMe	3,5-di-Cl-4-OH	379/381/383	1
A752	H	H	3-OMe	3,5-di-Br-4-OH	467/469/471	1
A753	H	H	3-OMe	3-CO2H-4-Cl	373/375	1
A754	H	H	3-OMe	3-CO2H	339	1
A755	H	H	3-OMe	3-OH	311	1
A756	H	H	3-NO2	4-CH2NH2	337 [M-H]-	10

A757	H	H	2-OMe	4-CH2NH2	322 [M-H]-	10
A758	H	H	3-Me	3,4-[S-CH=N]	336	1
A759	H	H	3-OMe	3,4-[S-CH=N]	352	1
A760	H	H	4-OH	3-CO2H-4-Cl	359/361	4
A761	H	H	4-NMe2	4-SMe	354	1
A762	H	H	4-Cl	3-OH-4-OMe	345/347	1
A763	H	H	3-NO2	4-(CH2)2CO2H	380[M-H]	1
A764	H	H	3-NO2	4-(CH2)2CO2Me	396	1
A765	H	H	4-Cl	4-(CH2)2CO2Me	385/387	1
A766	H	H	2-OMe	4-(CH2)2CO2H	367	1
A767	H	H	2-OMe	4-(CH2)2CO2Me	381	1
A768	H	H	4-Cl	3,5-di-Cl-4-Me	381/383/385/387	1
A769	H	H	4-Cl	4-trans-CH=CHCO2Et	397/399	1
A770	H	H	4-CO2Me	3-F-4-Me	355	11
A771	H	Me	4-Cl	2-Me	327/329	1
A772	H	H	3-NO2	4-[(CH2)2CONH(CH2)6-NHCOMe]	522	12
A773	H	H	4-Cl	4-[(CH2)2CONH(CH2)6-NHCOMe]	511/513	12
A774	H	H	2-OMe	4-[(CH2)2CONH(CH2)6-NHCOMe]	507	12
A775	H	H	3,5-di-Me	3,5-di-Cl-4-OH	377/379/381	1
A776	H	H	3,5-di-Me	3,5-di-Br-4-OH	465/467/469	1
A777	H	H	3,5-di-Me	3-CO2H-4-Cl	371/373	1
A778	H	H	3,5-di-Me	3-CO2H	337	1
A779	H	H	3,5-di-Me	3-OMe	323	1
A780	H	H	3,5-di-Me	3,4-[OCH2O]	337	1
A781	H	H	4-iPr	3,5-di-Cl-4-OH	391/393/395	1
A782	H	H	4-iPr	3,5-di-Br-4-OH	479/481/483	1

A783	H	H	4-iPr	3-CO2H-4-Cl	385/387	1
A784	H	H	4-iPr	3-CO2H	351	1
A785	H	H	4-iPr	3-OMe	337	1
A786	H	H	4-iPr	3,4-[OCH2O]	351	1
A787	H	H	2-Br	3,5-di-Cl-4-OH	427/429/431/433	1
A788	H	H	2-Br	3,5-di-Br-4-OH	515/517/519/521	1
A789	H	H	2-Br	3-CO2H	387/389	1
A790	H	H	2-Br	3-OMe	373/375	1
A791	H	H	2-Br	3,4-[OCH2O]	387/389	1
A792	H	H	3,4-di-OMe	3-OMe	355	1
A793	H	H	3-Cl-4-OMe	3,5-di-Cl-4-OH	413/415/417/419	1
A794	H	H	3-Cl-4-OMe	3,5-di-Br-4-OH	501/503/505/507	1
A795	H	H	3-Cl-4-OMe	3-CO2H-4-Cl	407/409/411	1
A796	H	H	3-Cl-4-OMe	3-CO2H	371/373 [M-H]-	1
A797	H	H	3-Cl-4-OMe	3-OMe	359/361	1
A798	H	H	4-Me	3,5-di-Cl-4-OH	363/365/367	1
A799	H	H	4-Me	3,5-di-Br-4-OH	451/453/455	1
A800	H	H	4-Me	3-CO2H	323	1
A801	H	H	4-Me	3-OMe	309	1
A802	H	H	4-Me	3,4-[OCH2O]	323	1
A803	H	H	2,4-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A804	H	H	2,4-di-Cl	3,5-di-Br-4-OH	503/505/507/509/511 [M-H]-	1
A805	H	H	2,4-di-Cl	3-CO2H	377/379/381	1
A806	H	H	2,4-di-Cl	3-OMe	363/365/367	1
A807	H	H	2,4-di-Cl	3,4-[OCH2O]	375/377/379[M-H]-	1
A808	H	H	3-Cl	3,5-di-Cl-4-OH	381/383/385/387[M-H]-	1
A809	H	H	3-Cl	3-CO2H	343/345	1

A810	H	H	3-Cl	3-OMe	329/331	1
A811	H	H	3-Cl-4-OMe	3,4-[OCH2O]	373/375	1
A812	H	H	3-Br	3,5-di-Cl-4-OH	425/427/429/431[M-H]-	1
A813	H	H	4-SMe	3,5-di-Cl-4-OH	393/395/397 [M-H]-	1
A814	H	H	4-F	3,5-di-Cl-4-OH	365/367/369 [M-H]-	1
A815	H	H	3-Cl	3,4-[OCH2O]	343/345	1
A816	H	H	4-Cl	3,4-[CO(CH2)4]	381/383	1
A817	H	H	4-Cl	3,4-[CH2SO2CH2]	387/389[M-H]-	1
A818	H	H	4-Cl	3,4-[O-C(Me)=N]	354/356	1
A819	H	H	4-Cl	3,4-[OCF2O]	379/381	1
A820	H	H	4-Cl	3,4-[O(CH2)3O]	371/373	1
A821	H	H	2,3-di-F	3,5-di-Cl-4-OH	383/385/387[M-H]-	1
A822	H	H	2,6-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A823	H	H	3,4-di-Cl	3,5-di-Cl-4-OH	415/417/419/421/423 [M-H]-	1
A824	H	H	2-F	3,5-di-Cl-4-OH	367/369/371	1
A825	H	H	2-Me	3,5-di-Cl-4-OH	363/365/367	1
A826	H	H	4-NO2	3,5-di-Cl-4-OH	392/394/396 [M-H]-	1
A827	H	H	3-OPh	3,5-di-Cl-4-OH	441/443/445	1
A828	H	H	4-OPh	3,5-di-Cl-4-OH	441/443/445	1
A829	H	H	3-NO2-4-Cl	3,5-di-Cl-4-OH	426/428/430/432 [M-H]-	1
A830	H	H	4-OH	3-Cl-4-OH	331/333	4
A831	H	H	4-OH	3-Br-4-OH	375/377	4
A832	H	H	4-Cl	4-trans-CH=CHCO2H	369/371	13
A833	H	H	4-Cl	4-trans-CH=CHCONH2	368/370	14
A834	H	Me	4-Cl	4-OMe	343/345	1
A835	H	H	3,4,5-tri-F	3,5-di-Cl-4-OH	401/403/405 [M-H]-	1
A836	H	H	2-NO2	3,5-di-Cl-4-OH	392/395/397 [M-H]-	1

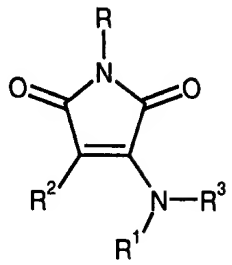
A837	H	H	3,5-di-F	3,5-di-Cl-4-OH	383/385/387 [M-H]-	1
A838	H	H	4-Cl	3-[OC6F5]	481/483	1
A839	H	H	4-Cl	2,3-[OCF2O]	377/379[M-H]-	1
A840	H	H	2-F	3,4-[S-CH=N]	340	1
A841	H	H	3-F	3,4-[S-CH=N]	340	1
A842	H	H	3-Cl	3,4-[S-CH=N]	356/358	1
A843	H	H	4-CF3	3,5-di-Cl-4-OH	415/417/419 [M-H]-	1
A844	H	H	3-SCF3	3,5-di-Cl-4-OH	447/449/451 [M-H]-	1
A845	H	H	4-OCF3	3,5-di-Cl-4-OH	431/433/435 [M-H]-	1
A846	H	H	3-CF3	3,5-di-Cl-4-OH	415/417/419 [M-H]-	1
A847	H	H	3,5-bis-CF3	3,5-di-Cl-4-OH	483/485/487 [M-H]-	1
A848	H	H	3,4-[OCH2O]	3,5-di-Cl-4-OH	393/395/397	1
A849	H	H	2-OCH2Ph	3,5-di-Cl-4-OH	455/457/459	1
A850	H	H	3,4-[(-CH=CH-)2]	3,5-di-Cl-4-OH	399/401/403	1
A851	H	H	4-Cl	3,4-[N=C(Me)-O]	354/356	1
A852	H	H	4-F	3,4-[S-CH=N]	340	1
A853	H	H	3-Br	3,4-[S-CH=N]	400/402	1
A854	H	H	2-Br	3,4-[S-CH=N]	400/402	1
A855	Me	H	4-Cl	3-CO2H-4-Cl	389/391/393 [M-H]-	1
A856	Me	H	4-Cl	4-CH2SO2NHMe	420/422	1
A857	Me	H	4-Cl	3,5-di-F	349/351	1
A858	Me	H	4-Cl	3,4-[OCH2O]	357/359	1
A859	Me	H	4-Cl	3,5-di-Cl-4-OH	397/399/401/403	1
A860	Me	H	4-Cl	4-(CH2)2CO2Me	399/401	1
A861	Me	H	4-Cl	4-(CH2)2CO2H	385/387	1
A862	H	H	4-COPh	3,5-di-Cl-4-OH	453/455/457	1
A863	H	H	3,4-di-F	4-SMe	347	1
A864	H	H	3,4-di-F	3,4-[(CH2)3]	341	1
A865	H	H	2,4-di-Cl	3,4-[S-CH=N]	390/392/394	1

A866	H	H	3,4-di-Cl	3,4-[S-CH=N]	390/392/394	1
A867	H	H	3-F	3,5-di-F	317 [M-H]-	1
A868	H	H	3-F	4-CH2SO2NHMe	390	1
A869	H	H	3-F	4-(CH2)2CO2H	355	1
A870	H	H	3-F	3-OMe	313	1
A871	H	H	3-F	3-Cl	317/319	1
A872	H	H	3-F	3-Cl-4-OMe	347/349	1
A873	H	H	3-F	3-Cl-4-OH	333/335	1
A874	H	H	3-F	4-(CH2)3CO2H	367 [M-H]-	1
A875	H	H	3-F	3,5-di-Me	311	1
A876	H	H	3-F	3-Cl-4-Me	331/333	1
A877	H	H	3-F	H	283	1
A878	H	H	2-Cl	3-F	315/317 [M-H]-	1
A879	H	H	2-Cl	3-OMe	329/331	1
A880	H	H	2-Cl	3-Cl-4-OMe	363/365/367	1
A881	H	H	2-Cl	3-Cl-4-OH	349/351/353	1
A882	H	H	2-Cl	4-(CH2)3CO2H	385/387	1
A883	H	H	2-Cl	3,5-di-OMe	359/361	1
A884	H	H	2-Cl	3-NO2-4-OH	360/362	1
A885	H	H	2-Cl	4-CH2P(O)(OEt)2	449/451	1
A886	H	H	2-Cl	4-NHCOMe	356/358	1
A887	H	H	2-Cl	4-(CH2)2CONH2	370/372	1
A888	H	H	2-Cl	3-CH2OH	329/331	1
A889	H	H	4-Cl	3-Cl-4-OMe	363/365/367	1
A890	H	H	4-Cl	3-Cl-4-OH	349/351/353	1
A891	H	H	4-Cl	3-CN	322/324 [M-H]-	1
A892	H	H	4-Cl	3-CO2Me	357/359	1
A893	H	H	4-Cl	2-Me-5-CO2Me	371/373	1
A894	H	H	4-Cl	3-Cl-4-Me	347/349/351	1

A895	H	H	3,4-di-F	3-CO2Me	359	1
A896	H	H	3,4-di-F	3-CO2H	343 [M-H]-	1
A897	H	H	4-Cl	2,3-[S-CH=N]	356/358	1
A898	H	H	4-Cl	3,4-[N=CH-S]	356/358	1
A899	H	H	4-Cl	3,4-[(CH2)2N(COMe)]	380/382[M-H]-	1
A900	H	H	4-Cl	3,4-[N(COMe)(CH2)2]	380/382[M-H]-	1
A901	H	H	3,4-di-F	3,4-[S-CH=N]	358	1
A902	H	H	4-Cl	3,4-[CH=CHCO-O]	367/369	1

Table B

Encompassing compounds of general formula (I) and substituents R, R^1, R^2 and R^3 are listed in Table B.



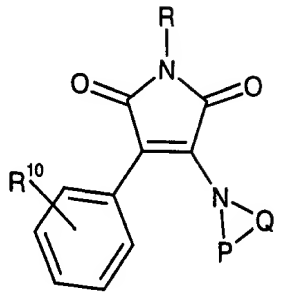
(I)

Example No.	R	R^1	R^2	R^3	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
B1	Me	Me	Indol-3-yl	Ph	332	3
B2	H	H	Indol-3-yl	H	228	5
B3	H	Me	Indol-3-yl	Ph	318	5
B4	H	H	Ph	H	189	1
B5	H	H	Ph	CH2Ph	279	1
B6	CH2Ph	H	Ph	CH2Ph	369	1
B7	H	Et	4-CF3-Ph	Et	313	1
B8	H	Me	4-OMe-Ph	CH2Ph	323	1
B9	H	Et	4-Cl-Ph	Et	279/281	1
B10	H	Me	4-Cl-Ph	CH2Ph	327/329	1
B11	H	Me	4-Cl-Ph	(CH2)2Ph	341/343	1

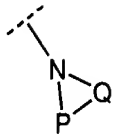
B12	H	Et	Ph	Et	245	1
B13	H	Me	Ph	CH2Ph	293	1
B14	H	Me	Ph	(CH2)2Ph	307	1
B15	H	(CH2)2OMe	4-Cl-Ph	(CH2)2OMe	339/341	1
B16	H	H	3-NO2-Ph	4-Me-Oxazol-2-yl	315	1
B17	H	Me	3-NO2-Ph	CH2Ph	338	1
B18	H	Me	3-NO2-Ph	(CH2)2Ph	352	1
B19	H	H	3-NO2-Ph	Cyclohexyl	314 [M-H]-	1
B20	H	H	2-OMe-Ph	Fluoren-2-yl	383	1
B21	H	H	3-NO2-Ph	Fluoren-2-yl	396 [M-H]-	1
B22	H	H	4-Cl-Ph	Dibenzofuran-2-yl	389/391	1
B23	H	H	4-Cl-Ph	Dibenzofuran-3-yl	389/391	1
B24	H	H	4-Cl-Ph	(2-Acetylbenzofuran-5-yl)	381/383	1
B25	H	H	3-NO2-Ph	H	234	16
B26	H	H	4-Cl-Ph	2,6-di-Me-pyridin-3-yl	328/330	13

Table C

Encompassing compounds of general formula (XXX-2), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and the moiety $-NR^1R^3$ of formula (I) represents a heterocyclyl moiety of general formula (XXX-3) and substituents R, R^{10} and P-Q are listed in Table C.



(XXX-2)



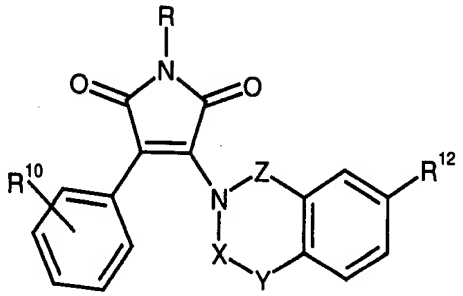
(XXX-3)

Example No.	R	R^{10}	P-Q	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
C1	H	4-OMe	(CH2)2O(CH2)2	289	1
C2	H	4-Cl	(CH2)4	277/279	1
C3	H	4-Cl	(CH2)2O(CH2)2	293/295	1
C4	H	4-Cl	(CH2)3CH(Me)CH2	305/307	1
C5	H	4-Cl	(CH2)3CH(CONH2)CH2	332/334[M-H]-	1
C6	H	H	(CH2)3CH(CONH2)CH2	300	1
C7	H	4-OMe	(CH2)3CH(CONH2)CH2	330	1
C8	H	H	(CH2)4	243	1
C9	H	4-Cl	(CH2)3CH(CH2OH)CH2	321/323	1
C10	H	4-Cl	(CH2)5	291/293	1

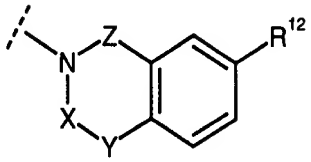
C11	H	4-Cl	(CH2)2CH(CH2Ph)(CH2)2	381/383	1
C12	H	4-Cl	(CH2)2CH(OH)(CH2)2	307/309	1
C13	H	3-NO2	(CH2)3CH(Me)CH2	316	1

Table D

Encompassing compounds of general formula (XXX-4), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and the moiety $-NR^1R^3$ of formula (I) represents a heterocyclyl moiety of general formula (XXX-5), optionally substituted by a substituent R^{12} and substituents R, R^{10}, R^{12}, X-Y and Z are listed in Table D.



(XXX-4)



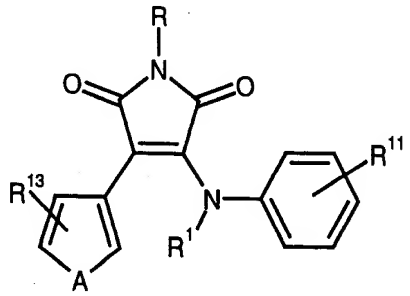
(XXX-5)

Example No.	R	R^{10}	R^{12}	X-Y	Z	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
D1	H	4-CF3	H	CH=N	bond	358	2
D2	H	4-Cl	H	(CH2)2	bond	325/327	1
D3	H	4-Cl	H	(CH2)2	CH2	339/341	1
D4	H	4-Cl	H	(CH2)3	bond	339/341	1
D5	H	4-Cl	NO2	(CH2)2	bond	370/372	1
D6	H	3-NO2	H	(CH2)2	CH2	350	1
D7	H	4-OMe	H	(CH2)2	bond	321	1
D8	H	4-Cl	H	(CH2)2	(CH2)2	353/355	1

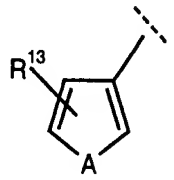
D9	H	3-NO2	H	(CH2)2	(CH2)2	364	1
D10	H	3-CF3	H	(CH2)2	bond	359	1
D11	H	3,5-di-F	H	(CH2)2	bond	327	1
D12	H	3-NO2	H	(CH2)2	bond	336	1
D13	H	2-OMe	H	(CH2)2	bond	321	1
D14	H	2-Cl	H	(CH2)2	bond	325/327	1
D15	H	2-OMe	H	(CH2)2	CH2	335	1
D16	H	2-OMe	H	CH(Me)CH2	bond	335	1
D17	H	2-Cl	H	CH(Me)CH2	bond	339/341	1
D18	H	3,5-di-F	H	CH(Me)CH2	bond	341	1
D19	H	3-NO2	H	CH=CH	bond	334	15
D20	H	3-NO2	H	CH(CO2H)CH2	bond	380	1
D21	H	3,4-di-F	H	(CH2)2	bond	327	1
D22	H	3-NO2	H	CH(CO2Me)CH2	bond	392 [M-H]-	1
D23	H	4-I	H	(CH2)2	bond	417	1
D24	H	3-Cl	H	(CH2)2	bond	325/327	1
D25	H	4-Br	H	(CH2)2	bond	369/371	1
D26	H	3-Br	H	(CH2)2	bond	369/371	1
D27	H	2-Me	H	(CH2)2	bond	305	1
D28	H	3-F	H	(CH2)2	bond	309	1
D29	H	2,4-di-Cl	H	(CH2)2	bond	359/361/363	1
D30	H	2-Br	H	(CH2)2	bond	369/371	1
D31	H	2-F	H	(CH2)2	bond	309	1
D32	H	4-COPh	H	(CH2)2	bond	394 [M]-	1
D33	H	2-NO2	H	(CH2)2	bond	336	1
D34	H	3,4,5-tri-F	H	(CH2)2	bond	343 [M-H]-	1
D35	H	2-OEt	H	(CH2)2	bond	335	1

Table E

Encompassing compounds of general formula (XXX-6), wherein group R^2 of formula (I) is a (3-heterocyclyl) moiety (XXX-7), optionally substituted by one or more substituents R^{13} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11} and R^{13} are listed in Table E.



(XXX-6)



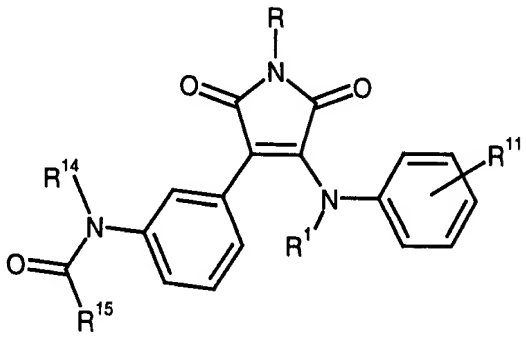
(XXX-7)

Example No.	R	R^1	R^{11}	R^{13}	A	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
E1	H	H	3-Br	4,5-[(-CH=CH-)2]	N(Me)	396/398	4
E2	H	H	4-Me	4,5-[(-CH=CH-)2]	N(Me)	332	4
E3	H	H	4-SMe	4,5-[(-CH=CH-)2]	N(Me)	364	4
E4	H	H	3-Br-4-Me	4,5-[(-CH=CH-)2]	O	397/399	4
E5	H	H	3-Br-4-Me	H	S	363/365	4
E6	H	H	3-Cl	H	S	303/305 [M-H]-	1

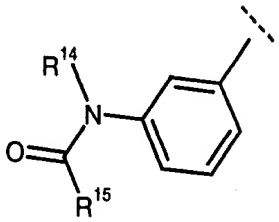
E7	H	H	3,4-[S-CH=N]	4,5-[(-CH=CH-)2]	N(Me)	375	4
E8	H	H	3-OPh	4,5-[(-CH=CH-)2]	N(Me)	410	4
E9	H	H	3,4-[(CH2)3]	4,5-[(-CH=CH-)2]	N(Me)	358	4
E10	H	H	3-SMe	H	S	315[M-H]-	1
E11	H	H	4-Me	H	S	283[M-H]-	1
E12	H	H	H	H	S	269[M-H]-	1
E13	H	H	3-OPh	H	S	361[M-H]-	1
E14	H	H	3,4-[(CH2)3]	H	S	309[M-H]-	1
E15	H	H	3-Br	H	S	347/349[M-H]-	1
E16	H	H	4-SMe	H	S	315[M-H]-	1
E17	H	H	3,5-di-Br-4-OH	H	S	441/443/445[M-H]-	1
E18	H	H	3-Cl	4,5-[(-CH=CH-)2]	S	355/357	1
E19	H	H	3,5-di-Cl-4-OH	H	S	353/355/357 [M-H]-	1

Table F

Encompassing compounds of general formula (XXX-8), wherein group R^2 of formula (I) is a moiety of formula (XXX-9), optionally substituted by substituents R^{14} and R^{15} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11}, R^{14} and R^{15} are listed in Table F.



(XXX-8)



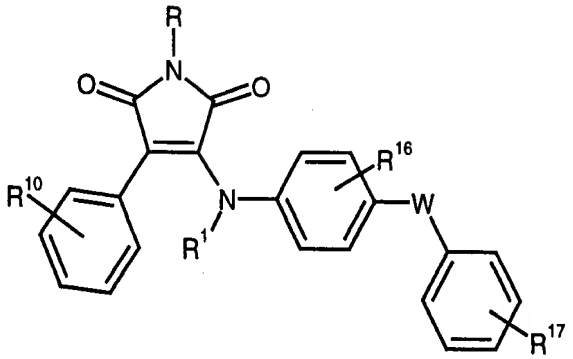
(XXX-9)

Example No.	R	R^1	R^{11}	R^{14}	R^{15}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
F1	H	H	3,4-[(CH2)3]	H	Me	360 [M-H]-	7
F2	H	H	3,4-[(CH2)3]	H	NH[3-F-Ph]	456 [M]-	8
F3	H	H	3,4-[(CH2)3]	H	NH(CH2)2Ph	467	8
F4	H	H	3,4-[(CH2)3]	H	NH[Cyclohexyl]	443 [M-H]-	8
F5	H	H	3,4-[(CH2)3]	H	NHCH2CH=CH2	403	8
F6	H	H	3,4-[(CH2)3]	H	Ph	422 [M-H]-	9
F7	H	H	3,4-[(CH2)3]	H	CH2Ph	436 [M-H]-	9

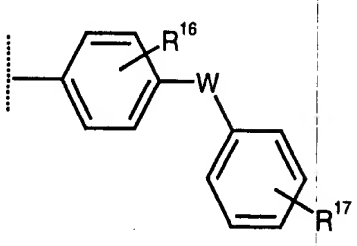
F8	H	H	3,4-[(CH2)3]	H	trans-CH=CHPh	450	9
F9	H	H	3,4-[(CH2)3]	H	n-Pr	390	9
F10	H	H	3,4-[(CH2)3]	H	NHEt	389 [M-H]-	8
F11	H	H	3,4-[(CH2)3]	H	NH[3-OMe-Ph]	469	8

Table G

Encompassing compounds of general formula (XXX-10), wherein group R^2 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{10} and group R^3 of formula (I) is a moiety of formula (XXX-11), optionally substituted by one or more substituents R^{16} and R^{17} and substituents R, R^1, R^{10}, W, R^{16} and R^{17} are listed in Table G.



(XXX-10)



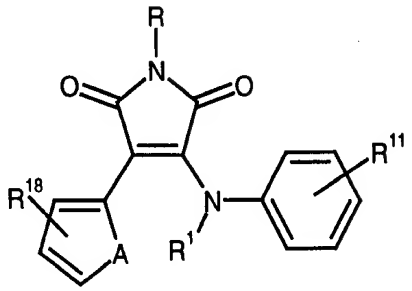
(XXX-11)

Example No.	R	R^1	R^{10}	W	R^{16}	R^{17}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
G1	H	H	2-OMe	S	3-CO2H	2-CO2H	491	1
G2	H	H	4-Cl	S	H	3-CO2H	449/451 [M-H]-	1
G3	H	H	4-Cl	S	3-CO2Et	2-CO2Et	550/552 [M]-	1
G4	H	H	4-Cl	S	3-CO2Me	4-Cl	497/499/501 [M-H]-	1
G5	H	H	4-Cl	S	3-CO2H	2-CONHMe	508/510	1
G6	H	H	4-Cl	S	H	4-NO2	450/452 [M-H]-	1
G7	H	H	4-Cl	O	H	4-Cl	425/427/429	1

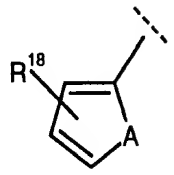
G8	H	H	4-Cl	S	H	2-CO2H	451/453	1
G9	H	H	4-Cl	S	3-CO2H	H	449/451 [M-H]-	1

Table H

Encompassing compounds of general formula (XXX-12), wherein group R^2 of formula (I) is a (2-heterocyclyl) moiety (XXX-13), optionally substituted by one or more substituents R^{18} and group R^3 of formula (I) is a phenyl ring, optionally substituted by one or more substituents R^{11} and substituents R, R^1, R^{11} and R^{18} are listed in Table H.



(XXX-12)

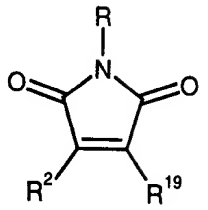


(XXX-13)

Example No.	R	R^1	R^{11}	R^{18}	A	$[M+H]^+$ Observed; (Unless $[M]^+$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
H1	H	H	3-Cl	H	S	305/307	1
H2	H	H	3-Cl	3-Me-4,5-[(-CH=CH-)2]	S	369/371	1
H3	H	H	3,5-di-Cl-4-OH	H	S	355/357/359	1

Table I

Encompassing compounds of general formula (XXX-14), wherein the moiety NR^1R^3 of formula (I) is represented by a general substituent R^{19} and substituents R, R^2 and R^{19} are listed in Table I.



(XXX-14)

Example No.	R	R^2	R^{19}	$[M+H]^+$ Observed; (Unless $[M]^-$ or $[M-H]^-$ are Indicated)	For Procedure see Example No.
I1	H	3-Thienyl	1-Indolinyl	297	1
I2	H	2-Thienyl	1-Indolinyl	297	1